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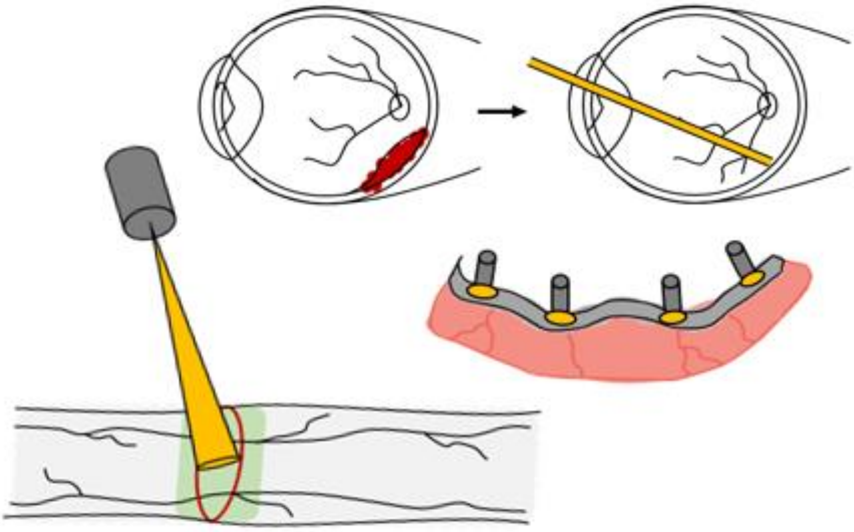

The applicability of welding technologies in the health sector: critical review

DIOGO FRANCISCO GOMES
(BSc in Mechanical Engineering)

Final Master's dissertation to obtain the Master's Degree in
Mechanical Engineering

Supervisors:
Dr. Ivan Rodolfo Pereira Garcia de Galvão
Dr. Maria Amélia Ramos Loja

Jury:
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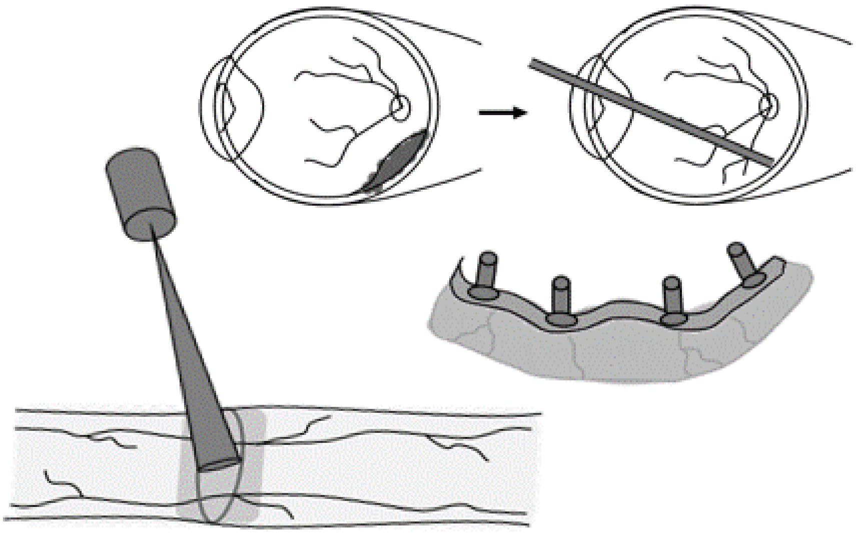

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ABBREVIATIONS/INITIALS

AFM	Atomic force microscopy
APC	Argon plasma coagulation
BSA	Bovine serum albumin
BCD	Bipolar electrocautery dissection
BSE	Bovine spongiform encephalopathy
CAW	Composite arch wire
CD	Cold dissection
CKD	Chronic kidney disease
CT	Computed tomography
DALK	Deep anterior lamelar kerotoplasty
DSEK	Descement’s stripping endophelial keratoplasty
DOF	Degree of freedom
DMA	Dental movement analysis
EC	Electrocautery
ED	Erectile dysfuction
ERW	Electrical resistance welding
FDA	Food and Drug Administration
FEM	Finite element method
FITC	Fluorescein isothiacyanate
HAZ	Heat-affected zone
HA3D^{TM}	Hyper-accuracy three-dimensional reconstruction
HF	Hydrogen fluoride
HFE	High frequency electrosurgical
HFEW	High frequency electrosurgical welding
IB	Infrared brazing
ICG	Indocyanine green
IR	Infrared
LASIK	Laser in situ keratomileusis
LAVA$_1$	Laser-assisted vascular anastomoses
LAVA$_2$	Laser-assisted vasovasostomy
LAVR	Laser-assisted vessel repair
LNW	Laser nerve welding
LTS	Laser tissue soldering
LTW	Laser tissue welding
LVSS	Ligasure vessel sealing system
LW	Laser welding
MCD	Monopolar electrocautery disseciton
MIAM	Multispectral imaging autofluorescence microscopy
MIS	Minimal invasive surgery
NIR	Near-infrared
PCL	Poly (ε - caprolactone)
PEG	Polyethylene glycol
PKP	Penetrating keratoplasty
PLGA	Poly (lactic-co-glycolic)
PLW	Pulsed laser welding
PRK	Photorefractive keratectomy
PTB	Photochemical tissue bonding
RB	Rose bengal
SLO	Scanning laser ophthalmoscope

SMILE	Small incision lenticule extraction
TB	ThunderBeat
TE	Tonsillectomy
TEM	Transmission electron microscopy
TFP	Thermal focal point
TO	Tonsillotomy
TSP	Tamarind seed polyssachride
TWT	Thermal welding tonsillectomy
UPS	Universal power supply
VAS	Visual analogue scale
vCJD	Creutzfeldt - Jakob disease

ABSTRACT

In early years, biological bonding of tissues was mainly made through suturing. Conventional sutures, despite being reliable and relatively inexpensive, have a direct relation to post-operative problems. With the purpose of eliminating these concerns, significant research on new surgical sutureless approaches has been conducted. The present work, which consists of a critical review research, is aimed to study sutureless approaches based on welding technologies. An analysis of their technological evolution, their advantages and drawbacks, and the phenomena occurring during their operation was conducted.

The integration of the welding technologies in the health sector, supported by innovative medical devices and new biomaterials, have led to the development of revolutionary photothermal and photochemical binding techniques. These techniques have presented improved results over the conventional mechanical techniques for tissue healing, with effect on a multitude of medical fields such as angiology, neurology, otolaryngology, ophthalmology, urology and dentistry. Medical parameters, such as post-operative pain, narcotics usage, tissue thermal response and operation time, have been significantly improved. Important work has been conducted to understand the biological tissue transformations and their relation to the temperatures reached during the processes. Actually, one of the most serious medical concerns associated with the implementation of welding techniques in health sector is the thermal damage. Many methods, such as temperature control feedback systems, saline solutions, mathematical models for prediction of temperature-tissue behaviours, biological solder solutions and dyes, have been developed to diminish or eliminate this concern. In this matter, the development of new image-processing techniques was also a major advance in the medical diagnosis and the anticipation of patient disease growth, with earlier surgical interventions and therapies. Furthermore, over the last 10 years, integration of robotics and nanotechnology enhanced biologic welding procedures with more efficient and safer intra-operative and post-operative procedures.

KEYWORDS: *Bioengineering; Welding technologies; Surgery; Tissue regeneration techniques.*

RESUMO

Antigamente, a ligação de tecidos biológicos era principalmente realizada através de suturas. Apesar de cumprirem a sua função e de serem relativamente de custo reduzido, as suturas convencionais encontram-se directamente relacionadas com problemas pós-operatórios. Com o propósito de eliminar quaisquer destes problemas, têm sido realizadas significativas investigações sobre novas abordagens cirúrgicas sem que seja necessário recorrer a suturas. O presente trabalho, que consiste numa revisão crítica, pretende estudar essas abordagens com base na aplicação de diferentes tecnologias de soldadura. Para isso, foi realizada uma análise em termos de evolução tecnológica, vantagens e desvantagens, bem como a caracterização do processo operatório.

A integração das tecnologias de soldadura no sector da saúde, suportada por dispositivos médicos inovadores e novos biomateriais, tem conduzido ao desenvolvimento de técnicas revolucionárias de ligação de tecidos, através do processo fototérmico e fotoquímico. Estas técnicas demonstraram resultados superiores comparativamente às técnicas convencionais para tratamento de tecidos, com efeito numa multitude de áreas médicas como a angiologia, neurologia, otolaringologia, oftalmologia, urologia e medicina dentária. Parâmetros médicos, como a dor pós-operatória, medicação, resposta térmica do tecido e o tempo de operação, têm sido significativamente melhorados. Foram realizados trabalhos importantes para compreender as transformações biológicas dos tecidos e a sua relação com as temperaturas atingidas durante os processos. Na realidade, uma das mais sérias preocupações médicas associadas com a implementação das tecnologias de soldadura no sector da saúde é o dano térmico. Vários métodos, como os sistemas de controlo de temperatura, soluções salinas, modelos matemáticos para a previsão de comportamentos térmicos dos tecidos, soluções de soldas e tintas biológicas, foram desenvolvidas para diminuir ou eliminar esta preocupação. Neste sentido, o desenvolvimento de novas técnicas de processamento de imagem foi também um grande avanço na realização do diagnóstico médico e na previsão de crescimento de doenças prejudiciais para os pacientes. Para além disso, durante os últimos 10 anos, a integração da robótica e a nanotecnologia melhoraram o processo de soldadura biológica através de procedimentos intra-operativos e pós-operativos mais eficientes e seguros.

PALAVRAS-CHAVE: *Bioengenharia; Tecnologias de soldadura; Cirurgia; Técnicas de regeneração de tecidos.*

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1. INTRODUCTION

The welding technologies are used all over the world in the production of the most diverse components for several sectors of activity. The demanding manufacturing strategies currently used in industry, which are focused on producing increasingly efficient components, must be supported by an ongoing optimisation of the joining processes. So, important research on welding technology is being conducted. As the widely-spread conventional fusion welding processes are no longer an effective solution for joining some materials and material combinations, the most explored research issue has been the optimisation of non-conventional welding processes, such as friction stir welding [1,2], ultrasonic welding [3,4], diffusion welding [5,6], magnetic pulse welding [7,8], laser welding, etc. Laser welding presents excellent characteristics, specifically, its accuracy and high-power density, enabling the production of highly localised welds, with minimal distortion and with a residual heat-affected zone (HAZ). So, laser welding of a large range of cutting-edge materials, such as NiTi shape memory alloys [9,10], Ni-based superalloys [11,12], and Ti alloys [13,14], and material combinations, such as Ta/Mo [15,16], NiTi/CuAlMn [17], NiTi/Ti [18], and Cu/Ti [19], has been intensively studied.

Welding technology is traditionally associated with industrial production. However, it is important to realise that the applications of welding, are not restricted to this field. The literature research herein conducted pretends to gather the relevant information about an innovative application of such technologies. These technologies have also presented a core position in the health sector [20–22]. The integration of welding technologies, in this sector, such as laser welding (LW) [23–25], ultrasound welding [26–28] or high frequency electrical welding (HFEW) [29,30], have promoted a revolution in medical practices by enabling the development of safer, earlier and faster surgical interventions and therapies [31,32]. Actually, medical parameters, such as post-operative pain, narcotics usage, tissue thermal response, and operation time, have been significantly improved [33,34]. Although welding technologies in the health sector are not recent, they remains a research topic with extreme relevance and actuality, since improved equipment, procedures and strategies have been developed in order to define optimised interventions that maximise the patient’s health [25,35]. Significant research on welding procedures has been conducted in a large range of medical areas, such as angiology [36,37], neurology [38,39], ophthalmology [40–42], otolaryngology [43,44], urology [45–47] and dentistry [48–50].

However, although important advances have been achieved in this field over the last 60 years, which have enabled to become welding procedures a common practice in surgeries, literature survey and review works on this issue are very incipient in literature. This way, the aim of the present research is to present an overview on the evolution of welding technologies in the health sector, particularly in angiology, neurology, otolaryngology, ophthalmology, urology and dentistry due to the extensive relevant studies published in these fields. The fundaments of the welding processes and the technological evolution registered, in which concerns to the equipment, materials and the adopted procedures and strategies, were analysed in this research. Additionally, literature research was conducted through the access to online scientific libraries with a two-phase keyword refinement.

The present research document enabled the author to participate in the scientific conference "*6th ENBENG – IEEE Portuguese Meeting on Bioengineering"*, with the presentation of the poster *"WELDING TEHCNOLOGIES IN THE HEALTH SECTOR"*. It also enabled the production of the paper *"OVERVIEW ON THE EVOLUTION OF LASER WELDING OF VASCULAR AND NERVOUS TISSUES"*, which was submitted to a scientific journal indexed in *Web of Science*. This paper is currently under review. Two other scientific papers are being written to be submitted soon to different journals, also indexed in *Web of Science*. This was the main reason for writing this document in English, since it enables an easier and wider dissemination of its main results and conclusions.

Finally, the document is structured in five main sections each one presenting the review of welding technologies in the previously mentioned health sectors. It begins by presenting the angiology and neurology sectors, followed by otolaryngology, ophthalmology, urology and concludes with dentistry welding technologies applications. Following these sections, an overall discussion is presented as well as the main conclusions and suggestions for future research in this field.

2. METHODOLOGY

The conducted literature research, for the elaboration of the present work, followed an organized research methodology with posterior treatment of relevant information (**Fig. 1**). The definition of essential research factors such as the idiom, used keywords, search engines, Boolean operators and research time intervals were determinant for the collection and analysis of reliable and relevant studies.

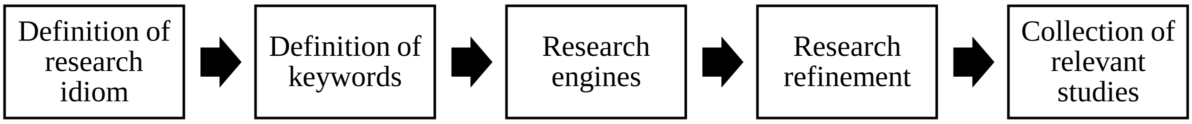


Fig. 1 – Literature research methodology for collection of relevant studies.

When following **Fig. 1** methodology, and considering the relevance of the approached topic in the scientific community, it was decided that the English idiom would be the most suitable due to its universality and to the fact that the main published scientific papers are in this idiom as well.

In a primary phase of research, general topic keywords were defined so that it would be possible to evaluate the main relevant areas of the health sector in which welding technologies were adopted. After this initial research, a second phase was conducted due to the increased familiarity with specific terms of each medical section, and so research refinement was made. These phases of literature research and respective keywords are exposed in **Table 1** and **Table 2**.

Table 1 - Keywords applied in 1st research phase.

1st research phase keywords			
Welding	Regeneration	Laser	Nanomedicine
Repair	Bonding	Device	Robotic surgery
Tissue	Biologic	Thermal	Nanotechnology
Weld	Biocompatibility	Health	Sutureless repair
Surgery	Biomedicine	Fusion	Technique
Welding technologies	Organ	Bioengineering	Method

Table 2 - Keywords applied in 2nd research phase.

2nd research phase keywords				
Angiology and Neurology	**Otolaryngology**	**Ophthalmology**	**Urology**	**Dentistry**
Nerve repair	Welding	Eye surgery	Urology welding	Oral tissues
Vascular	Tonsillectomy	Cornea weld	Urinary tract reconstruction	Hard tissues
Welding	Thermal welding	Ocular tissue welding	Endourology welding	Mandibular weld
Artery	Laser tonsillectomy	Femtosecond lasers	Vasectomy	Dentistry lasers
Neurology	Otolaryngology welding	Eye laser welding	Bladder welding	Orthodontic
Veins	Thermal fusion	Retina weld	Urethra welding	Prosthodontic
Photocoagulation				Intraoral weld

In terms of time interval definition and type of publication, research refinement was achieved with no chronologic limitations and mostly centred in journal scientific articles and published book sections. This way, it was possible to create a solid and global overview of the welding technologies role in each medical area studied, with reliable sources of scientific relevance. The scientific data was collect from online scientific libraries such as the *Web of Science*, *Science Direct*, *Wiley Online Library*, *B-on*, *Springerlink*, *American Urological Association – The Journal of Urology*, *SPIE Digital Library*, etc. The collected relevant studies were treated and organized with the *Mendeley* software. Additionally, the process of information treatment was carefully designed (**Fig. 2**) since the gathered literature complied multiple applications of welding technologies within the health sector.

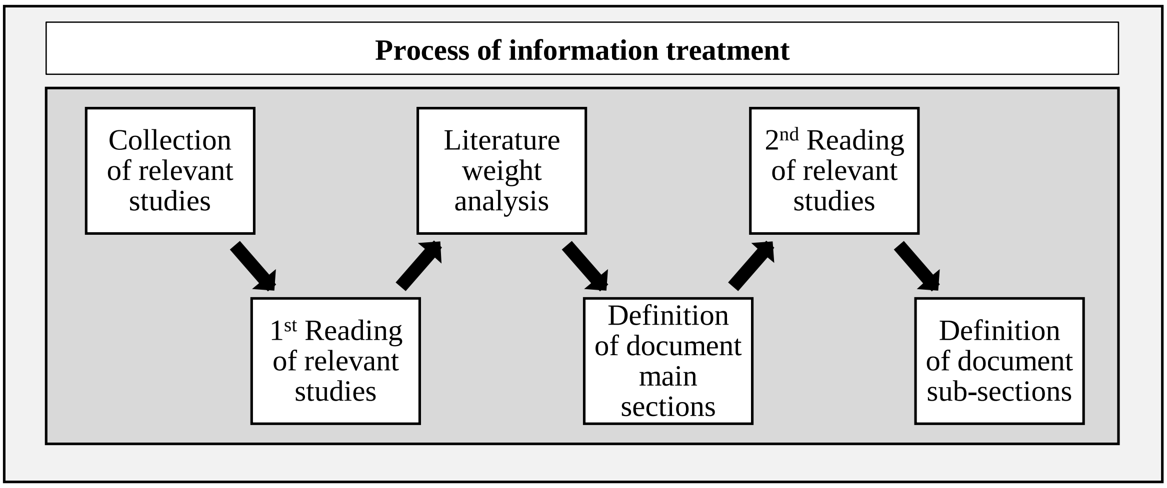


Fig. 2 - Process of information treatment.

In a first approach, the reading of each scientific paper or book section was made with consequent attribution of the medical area in which it was inserted. A literature weight analysis of the relevant medical areas to be studied was then carried for the categorization of the document main sections. The next step in this process was a second detailed reading and analysis for the definition of possible document sub-sections. In this matter, the organization of relevant information in scheme structures allowed a simplified comprehension of the collected data for possible results intersection of the defined sub-sections and respective main sections. The present research framework herein exposed was the result of this thorough process (**Fig. 2**).

3. ANGIOLOGY AND NEUROLOGY

The nervous system is formed by a central system which is responsible for total control of the nerves, transmitting signals to the peripheral nervous system. The peripheral nervous system receives these signals and distributes the different stimulus to the neuronal circuits, more precisely to the nerve cells. In turn, the circulatory system is formed by two distinct circuits: the systemic circuit and the pulmonary circuit, both presenting arteries and veins that distribute the blood to every organ and muscle.

In these two medical fields different injury reconstruction and repair techniques for nerves, arteries and veins, can be applied. The success of this type of surgery depends on various factors such as the gravity of the injury, the applied surgical technique, the surgeon experience and the post-operative biological response [39]. In most common surgeries (arteriotomies, venotomies, arteriovenous fistulas and nerve coaptations) the repair is completed recurring to conventional sutures although there are already different reconstructive techniques that oppose their application, with improved operative and post-operative results, as shown in **Table 3**.

Table 3 - Techniques for nerve, arteries and veins repairs.

Techniques for nerve, arteries and veins repairs		
Conventional techniques	Suture	Nonabsorbable suture [51–53]
		Absorbable suture [51]
Non-conventional techniques	Laser welding	Argon laser welding [51,54]
		CO_2 laser welding [37,38,54,55]
		Nd:YAG laser welding [54]
		Infrared diode laser welding [56,57]
		Potassium titanyl phosphate laser welding [23]
	Laser welding with intraluminal light source [58]	
	Photochemical tissue bonding [39,59–61]	
	High frequency electrosurgical welding [30]	

Conventional sutures are reliable and relatively inexpensive, however, through the years, various studies [39,51,52,55] concluded that there is a direct relation between sutures and post-operative biological problems, such as foreign body reactions, intimal hyperplasia and anastomotic stenosis. With the objective of minimizing these problems, but still applying a suture approach, Lawrence *et al.* [51] presented a study that demonstrates and compares the application of absorbable sutures and conventional sutures. The results showed similar burst strengths with absorbable sutures presenting an excellent recovery of the blood vessel wall with minimal inflammatory modifications.

Prior to the use of absorbable sutures in Lawrence *et al.* [51] study, the medical evolution had already shown results towards a sutureless approach with the integration of laser in medical surgeries. Repair of blood vessels with Nd:YAG laser was achieved in 1979 [59,62] and, seven years later, laser welding nerve coaptations were successfully reported by White *et al.* [54,63]. The results of these two studies proved the advantages of laser welding, which have already been corroborated by recent literature [64]: increasing accuracy with minimum tissue damage, decreasing operative time, preventing foreign-body reactions and reduction of the formation of post-operative aneurysms. Although laser welding is a technique with many advantages, various studies had verified that it also requires a strong surgical experience to achieve successful results [23,51,55].

The research and findings on sutureless approaches are addressed in this section, demonstrating different techniques for nerve, artery and vein repairs and focusing on their evolution over the last 40 years.

3.1. Laser welding technique

Laser welding technology was a major development in the innovation of vascular and nervous repair techniques as far as efficiency and precision are concerned. Although it has been verified that laser thermal damage occurs and according to Menosky *et al.* [55] and Happak *et al.* [38], there are rates of dehiscence between 12% and 41%, resulting from the bonding low tensile strengths. It is possible to minimize these factors by controlling the parameters and variables of laser welding. Variables such as laser wavelength, depth of tissue penetration, energy fluency, tissue absorptive characteristics and the laser exposure time as well as the application of cooling solutions to diminish neural, artery and vein thermal degeneration, will influence the success of the repair [39,54,55].

In most arteriotomies and venotomies, traction sutures are placed to approximate the vessel edges, improving the probability of welding success by assuring the bonding strength of the procedure [37,52,63,65,66]. Nakadate *et al.* [56] proved the beneficial effect of preloaded longitudinal compression on the weld strength, in laser-assisted vessel repair (LAVR) verifying a success rate of 83% when compared to welds where preloaded compression was absent. Instrumentation utilized by Nakadate *et al.* [56] is illustrated in **Fig. 3**, demonstrating a prototype of a vessel clamp device (**Fig. 3a**) used for compression application in pre-operative welding repair (**Fig. 3b**).

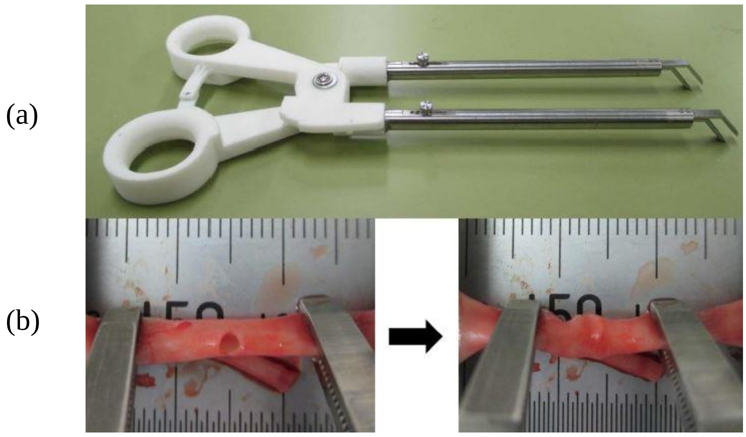
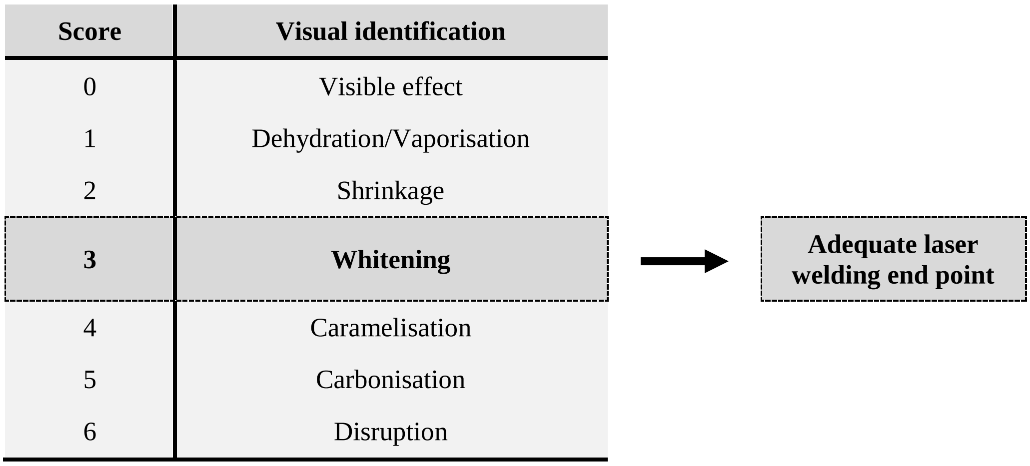


Fig. 3 - Instrumentation for preloaded longitudinal compression: (a) Vessel clamp device (prototype); (b) Procedure of preloaded longitudinal compression [56].

After this primary stage, the laser welding application occurs when laser energy, due to its capability for selective modulation of the biologic functions of cells, focuses on structural proteins resulting in the protein denaturation process at temperatures between 60ºC and 65ºC [54,65–67]. When the temperature exceeds 65ºC, the fusion with laser will not serve its purpose and cell degeneration will take place, primarily through vaporisation at 100ºC and finally through burn or disruption at higher temperatures [51,54,65,67]. Thus, it is important to use lower laser powers, increasing the time of exposure to achieve the cross-linking fusion of collagen fibrins which, according to White *et al.* [54], Lawrence *et al.* [51], Hasegawa *et al.* [52] and also Korsak and Chaikovskii [30], are directly related to the success of the welding operation. Otherwise, the extensive thermal damage implies cells permanent damage, i.e. without possible regeneration. It is also important to take into consideration tissue apposition, i.e. the position of adjacent tissues where the welding procedure will be applied, as it will determine the quality of the bonding of collagen fibrins [55,65,66]. In a final stage, it is necessary to analyse the end point of laser welding application through visual feedback, which is the most common method. Chuck *et al.* [68] and Menosky *et al.* [55] created visual identification scores for correlation of the response of the welded tissue with different argon-laser setting parameters and the resulting weld end points, respectively. **Fig. 4** shows the stages of welded end points, being the "whitening" and the "beginning of caramelization" the most adequate appearances [37,55,66,68].



Score	Visual identification
0	Visible effect
1	Dehydration/Vaporisation
2	Shrinkage
3	**Whitening**
4	Caramelisation
5	Carbonisation
6	Disruption

Adequate laser welding end point

Fig. 4- Visual identification scores and adequate laser welding end point (built based on data from [55, 68]).

All these methods for end point identification are associated with the prevention of laser welding thermal damage and consequently the prevention of vessel wall weakening [58]. Thermal tissue degeneration is directly related with laser parameters and biological conditions, mainly with time of laser exposure and the absorptive properties of the intervention region. An equilibrium of these factors is crucial to achieve improved results, in this matter [37,57]. Several strategies have been tested in laser welding procedures in order to achieve better welding conditions, such as the use of thermal feedback systems, saline solutions, and different irradiation techniques. The most reported method consists of measuring the temperature using thermal feedback systems [52,55].

The use of thermal feedback systems is a very effective strategy for preventing the thermal damage, as they enable the monitoring of the temperature in the weld region, with a very precise control of the laser parameters [37,52,55,59,66]. Regarding the use of saline solutions, although Menosky *et al.* [55] reported that they could decrease the bonding strength of the weld, many other studies demonstrated that it had no implications on this property, being an effective strategy for cooling down the welding site [51,52,63,65]. Another strategy was tested by Pabittei *et al.* [67], who compared different irradiation techniques in vascular repairs, specifically, laser welding scanning and single-spot laser welding. According to these authors, the single-spot method may be more beneficial when applied through multiple laser pulses in the surgical area, enabling tissue cool down between pulses, and therefore, decreasing the thermal damage. Research has also been conducted to predict tissue damage and the corresponding tissue effect by a finite element method (FEM), which may provide useful pre-operative information to the laser welding procedure [69].

3.1.1. Tensile strength and complementary sutures

As previously mentioned, the fusion of cross-linking collagen fibres is the main responsible for the weld bonding strength [38]. The bonding strength of the weld will determine if the procedure was successful. So, it is necessary to perform measurements of vascular seal resistance to intraluminal pressurisation taking into consideration the systolic blood pressure [64]. With the purpose of comparing tensile strength of both suture and laser-welding techniques, tensile strength measurements are made on the specimens. These evaluations were already considered in initial studies by White *et al.* [63,65], where the load at breaking of vessel walls in welded arteriovenous surgical sites were found to be effective compared to normal arteries and veins, as shown in **Fig. 5**.

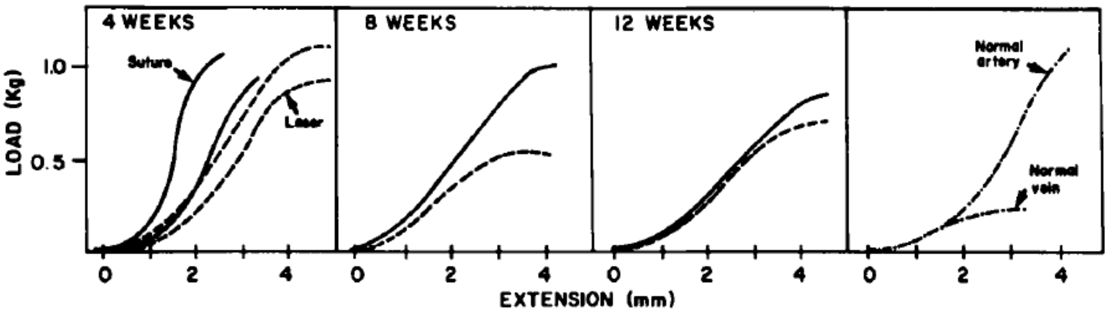


Fig. 5 - Tensile strength of artery-vein anastomoses by suture and laser welding [65].

Although White *et al.* [63,65] presented positive results for laser welding in respect of tensile strength, they also confirmed that additional sutures were required to achieve them. In this matter, the following table (**Table 4**) summarises previous results of laser welding procedures in which additional sutures were applied. More recently, Jonge *et al.* [37], Barton *et al.* [39] and Kramer and Rentschler [64] refer that many surgeons still apply additional sutures when using laser welding techniques in the repair procedure. Analysing and observing the various studies mentioned and the practices involved in each one of them, it is possible to verify that sutures keep being a support for the laser welding technique success.

Table 4 - Laser welding with complementary sutures in vascular and nerve surgeries.

Study	Total No. of welds	No. of welds with complementary sutures	No. of additional sutures per weld
White *et al.* [54]	5[a]	1	1
White *et al.* [63]	12	12	1
White *et al* [65]	24	12	1 to 2
Lawrence *et al.* [51]	61	55	1
Hasegawa *et al.* [52]	12	8	1 to 3

a - only the welds produced with argon laser were considered.

3.1.2. Overview of nervous and vascular repairs

The most commonly used medical lasers are CO_2, argon and Nd:YAG. The CO_2 and argon lasers are those with the most suitable application in medical surgeries due to their laser properties and their biological compatibility [38,39,51,66]. The application of these lasers is characterised by their coagulation, vaporisation and disruption capabilities [54]. By 1986, White *et al.* [54], demonstrated and compared laser welding of four millimetres thick-walled arteries with CO_2, Nd:YAG and argon lasers for the purpose of histological examination. Taking into consideration the results of this study, the evolution of LW in this field and laser properties, it is possible to define the most suitable surgical applications for each type of laser. Thus, the principal applications, advantages and drawbacks of CO_2, argon and Nd:YAG lasers are displayed in **Table 5**.

Table 5 - Argon, CO_2 and Nd:YAG characteristics in vascular and nerve laser welding repairs.

Laser	Suitable surgeries	Advantages	Drawbacks
Argon	Vascular repairs	Deep vessel wall penetration with lower energy output [51]	Nerve absorption of laser light is minimum due to lack of presence of significant chromophores. [66]
CO_2	Nerve repairs	High energy output [51] Low penetration depth [55]	Used primarily to cut and vaporise tissue [54] Low strength in arterial repairs, cannot sustain systemic pressures [63]
Nd:YAG	Vascular repairs	Easily penetration of the tissue [54]	Limited to microvascular anastomoses surgeries [51] Produces deep uncontrolled thermal injury due to excessive energy density [54] Low strength in arterial repairs, cannot sustain systemic pressures [63]

In respect of vascular argon-laser welding repair, the results are mainly superior when compared to conventional suture application. White *et al.* [54] also revealed that the biological effects of argon-laser welding in vascular healing presented minimal inflammatory response, near normal collagen content and no aneurysm formation. The optimal vascular results of argon laser welding were corroborated along the years by other authors [51,52,63,65]. Nervous CO_2 laser welding repairs also presented evolutionary results. Specifically, Bhatt *et al.* [23], in a recent study, concluded that CO_2 laser welded nerve coaptations can be performed with higher functional recovery rates than those achieved by nerve sutures. A chronological overview of the verified histological examination with argon and CO_2 laser procedures is summarised in **Table 6**.

Table 6 - Overview of histological results of CO_2 and argon repairs over conventional suturing.

Study	**Laser Welding**		**Histologic examination**
	CO_2	**Argon**	
White *et al.* [54]	-	x	Minimal inflammatory response, near normal collagen content, absent of aneurysm formation.
White *et al.* [63]	-	x	Absent of hematomas, false aneurysms or luminal dilatation and minimal inflammatory response.
White *et al.* [65]	-	x	Minimal inflammatory response and near-normal collagen content.
Lawrence *et al.* [51]	-	x	Absent aneurysm formation.
Menosky *et al.* [55]	x	-	Absent foreign body reaction, minimised scar tissue formation.
Happak *et al.* [38]	x	-	Minimised tissue thermal damage and no foreign body reactions
Hasegawa *et al.* [52]	-	x	Absent aneurysm formation although with no complete regeneration of the elastic lamina.
Jonge *et al.* [37]	x	-	Minimal thermal necrosis and welding strength increase.
Bhatt *et al.* [23]	x	-	Good functional recovery with no nerve dehiscence.

Despite the focus on CO_2 and argon in LW techniques, recent studies by Leclère *et al.* [62] and Nakadate *et al.* [56], showed that the use of infrared (IR) diode lasers can be innovative and excellent alternatives. At wavelengths of 1,450, 1,940 and 1,950 nm, water presents high absorption coefficients, which enables to perform laser welding repairs without recurring to a chromophore or solder solution and still obtaining good surgical results such as minimal aneurysm formation. Another alternative to CO_2 and argon laser welding could be the potassium titanyl phosphate (KTP) laser welding technique which, according to Bhatt *et al.* [23], has better functional recovery than CO_2 laser welding, i.e. 92.4% against 86.8%.

These correlations between the type of surgery, laser applied and the setting parameters can be observed through the medical evolution in this field. **Table 7** presents an overview of the main researches conducted in vascular and nervous laser welding over the last 30 years. The laser type and the main parameters tested in these works are displayed in the table. The research has been mainly focused on optimising the inverse relation existing between the laser power and the exposure time by testing different laser types (different wavelengths). Both approaches, i.e. lower power/higher exposure time and higher power/lower exposure time, have been tested in literature. However, the tested conditions are not generally applicable, since they strongly depend on the specific application, and consequently, on the interaction mechanisms between the laser radiation and the welded tissues. The application of external bonding materials, protein solutions (solders), and dyes in the weld region has also been intensively studied.

Table 7 - Chronological overview of laser welding results in vascular and nerve repair.

Study	**Surgery**	**Laser type**	**Welding parameters**			
			Wavelength (nm)	**Power (W)**	**Spot size (cm^2)**	**Exposure time (s)**
White *et al.* [54]	Vascular	Argon	458-515	1.5	0.07	300-400
		CO_2	10,600	1-2	0.03	20-40
		Nd:YAG	1,060	7	0.03	20-25
White *et al.* [63]	Vascular	Argon	NR.	0.5	0.066	240
White *et al.* [65]	Vascular	Argon	NR.	0.5	0.066	125-150
Chuck *et al.* [68]	Vascular	Argon	488	0.01-0.03	0.007	15-120
Lawrence *et al.* [51]	Vascular	Argon	NR.	0.75	0.07	100
Menosky *et al.* [55]	Nerve	CO_2	NR.	0.05-0.015	0.001	0.1-3
Curtis *et al.* [53]	Nerve	IR diode	810	0.08	NR.	NR.
Happak *et al.* [38]	Nerve	CO_2 w/ power reduction unit	NR.	0.06	0.0002	NR.
Hasegawa *et al.* [52]	Vascular	Argon	NR.	0.17	0.005	5
Stewart *et al.* [70]	Vascular	IR diode	808	0.08	0.02	0.5
Ott *et al.* [58]	Vascular	IR diode	808	0.41	0.1-0.27	30
				0.55		45
O'Neill *et al.* [59]	Vascular	PTB w/ Nd:YAG	532	0.35	1	300

N.R. – Non-referred.

Table 7 - Chronological overview of laser welding results in vascular and nerve repair (*Cont'd.).*

Study	Surgery	Laser type	Welding parameters			
			Wavelength (nm)	Power (W)	Spot size (cm^2)	Exposure time (s)
Jonge *et al.* [37]	Vascular	CO_2	10,600	0.17	0.012	261±40
Bogni *et al.* [36]	Vascular	IR diode	808	NR	0.21	NR
Pabittei *et al.* [67]	Vascular	IR diode Single-spot	670	1.6	1.3	50
		IR diode Scanning			0.27	82
Pabittei *et al.* [57]	Vascular	IR diode	670	0.096	0.08	25
Nakadate *et al.* [56]	Vascular	IR diode	970	2.4	0.01	30
Bhatt *et al.* [23]	Vascular	CO_2	10,600	0.1	NR	1
		KTP	532	3-4	NR	1
Hiebl *et al.* [71]	Vascular	IR diode	808	0.25-1.5	NR	30

N.R. – Non-referred.

3.1.3. Solders and laser-activated dyes

The high dehiscence rates were one of the main drawbacks in laser welding repairs therefore, in order to overcome this obstacle and achieve sutureless welds without dehiscence, external bonding materials and protein solutions were added to the procedure, reducing thermal damage and improving the tensile strength of the weld [38,53,67,70]. Menosky *et al.* [55] concluded, and Hiebl *et al.* [71] recently confirmed, that the amount and concentration of structural proteins were directly correlated with the bonding strength of the welded repair. These protein solutions are also known as solders. The various types of solders and bonding materials that can be applied to nervous and vascular repairs are exposed in **Table 8**. In initial studies biodegradable glues were applied with success however, the development of albumin-based solution solders allowed higher biocompatibility between its proteinaceous structure and collagen fibres. Being possible its application with different composition variations, this solder solution is the most common in these procedures [38,39,67,70].

Additionally, from **Table 8** it is possible to observe that, despite the reduced inflammatory reactions and easy application, biodegradable glues (fibrin and cyanoacrylate glues) should be avoided due to their rigidity, cytotoxicity and risk of infection formation [39,58,64]. Parallel to fibrin glues and cyanoacrylate glues, BioGlue can also be applied, presenting a composition of 45% bovine serum albumin (BSA) and 10% glutaraldehyde which cross-links with tissue fibres through chemical bindings allowing vascular chemical stabilisation of sutured and welded sites [64].

Table 8 - Solders and bonding materials characteristics in vascular and nerve repairs.

Solders and bonding materials	Advantages	Drawbacks
Fibrin glue [39]	Reduces inflammatory tissues and easy application	Low tensile strength, infection risk
Cyanoacrylate glue [39,64]	High tensile strength and easy application	Requires support stay sutures, causes fibrosis, foreign body toxicity
Polyethylene glycol (PEG) [39]	Nontoxic, biocompatible and reduces scar tissue	Slow degradation process (over 20 months)
Albumin-based solution [37,39,71]	In nerve repairs, protects the epineurium, increases bonding strength, reduces thermal damage	Leakage of fluid solder, thermal damage still present, becomes brittle

Over the last 25 years, important research has been conducted on the application of solder solutions in vascular and nerve medical procedures. Menosky *et al.* [55] compared different types of solders with the laser nerve welding (LNW) technique, observing an increased bonding strength with dried albumin, 20% of albumin and egg white solutions, when compared with LNW alone and fibrin glue repairs. It was also concluded that there was no improvement in bonding strengths with an application of 5% of albumin solution. By 1998, Curtis *et al.* [53] confirmed these findings by demonstrating that leakage of liquid solder solutions occurred during surgery which created an obstacle in the regeneration process. In agreement with this, Jonge *et al.* [37] observed that the disruption of low viscosity solder solutions occurred at the solder midline. However, regarding to semi-solid solder solutions, the same authors reported that these solutions withstand higher pressures in the solder area than at the interface, due to higher protein concentrations. The application of a semi-solid solder solution in arterial laser welding is illustrated in **Fig. 6**. As illustrated by the black dots, although LW is a highly localised process, a heat affected zone was generated around the welding site, which agrees well with the aforementioned concerns regarding to thermal damage.

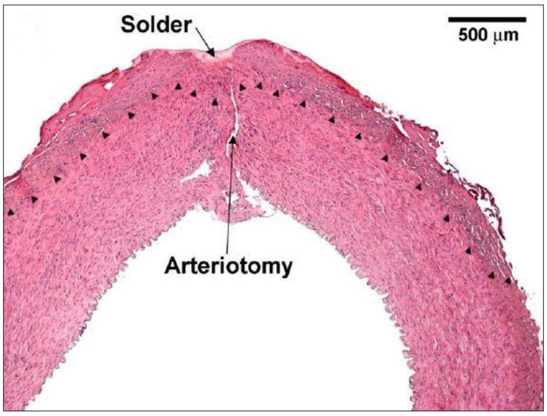


Fig. 6 - Transverse cross-section of a repaired artery by laser welding, with the application of a semi-solid solder solution [37].

Bogni *et al.* [36] and Pabittei *et al.* [67] focused on minimizing solder leakage by utilizing biodegradable polymers as carrier material for the liquid solder and by studying solder viscosity, respectively. In 2014, Pabittei *et al.* [57] confirmed the results demonstrated by the three previous studies mentioned, concluding that porous polymer scaffolds prevent solder leakage and also that the application of a semi-solid solders would provide higher protein density and cohesive bonding due to their flexible properties when compared to fluid solders. With the integration of solders in vascular and nervous laser repairs, it was also possible the extrapolation of diverse techniques to improve the process. Stewart *et al.* [70] introduced heparin in an albumin-based solder with the purpose of reducing microvessel thromboses that consequently occur with the laser welding procedure. In turn, Barton *et al.* [39] confirmed the possibility of including support cross-linking agents, such as genipin, in albumin-based solders to improve their flexibility and reduce brittleness. This “carrier” function is still a suitable and viable option and in a recent study, Hiebl *et al.* [71] used carrier membranes with BSA solder and indocyanine green (ICG) dye to improve bonding strength and prevent liquid solder leakage, with positive results.

On another perspective, Chuck *et al.* [68] and Curtis *et al.* [53] applied laser-activated dyes in solder solutions, such as fluorescein isothiacyanate (FITC) and ICG, which enhanced the bonding strength with lower energy outputs, due to selective laser absorption, and minimised associated thermal damage with improved visualisation of the weld site. Furthermore, Ott *et al.* [58] and Hiebl *et al.* [71] used ICG dyes in LW microvascular repairs also verifying that laser-activated dyes are of great importance for the achievement of better procedure outcomes. An overview of these results achieved with laser welding in vascular and nervous repairs is summarised in **Table 9**, which derives from **Table 7** with the inclusion of the different solder solutions applied and the respective remarks of the studies exposed so far.

Table 9 - Overview of laser welding results in vascular and nerve repair.

Study	Surgery	Type of laser	Solder + Dye	Welding parameters				Remarks
				Wavelength (nm)	**Power (W)**	**Spot size (cm^2)**	**Exposure time (s)**	
White *et al.* [54]	Vascular	Argon	NR.	458-515	1.5	0.07	300-400	Argon laser welding is suitable for healing of 4-6 mm arteries with no aneurysm formation.
		CO_2	NR.	10,600	1-2	0.03	20-40	
		Nd:YAG	NR.	1,060	7	0.03	20-25	
White *et al.* [63]	Vascular	Argon	NR.	NR.	0.5	0.066	240	Argon laser welding is suitable for healing of 4-8 mm arteries with no aneurysm formation.
White *et al.* [65]	Vascular	Argon	NR.	NR.	0.5	0.066	125-150	Argon laser welding occurs with fusion of collagen fibres and is preferred to suture techniques.
Chuck *et al.* [68]	Vascular	Argon	FITC	488	0.01-0.03	0.007	15-120	FITC application minimised thermal damage and allowed localised energy deposition.
Lawrence *et al.* [51]	Vascular	Argon	NR.	NR.	0.75	0.07	100	$LAVA_1$ with longer operative time. High control repair and expensive procedure over absorbable sutures.
Menosky *et al.* [55]	Nerve	CO_2	Dried BSA solution	NR.	0.05-0.015	0.001	0.1-3	LNW with solder solution has shorter operative time over LNW alone and suture techniques.
Curtis *et al.* [53]	Nerve	IR diode	BSA solution w/ ICG	810	0.08	NR.	NR.	Primary results for inferior alveolar nerve repair. LNW technique w/ lower operative time and good histological results.
Happak *et al.* [38]	Nerve	CO_2 w/ power reduction unit	NR.	NR.	0.06	0.0002	NR.	Advantageous results achieved with CO_2 LNW.
Hasegawa *et al.*[52]	Vascular	Argon	NR.	NR.	0.17	0.005	5	Laser welding with no aneurysm formation and complete regeneration.

$LAVA_1$ – Laser-assisted vascular anastomoses
NR. – Non referred.

Table 9 - Overview of laser welding results in vascular and nerve repair (*Cont'd*).

Study	Surgery	Type of laser	Solder + Dye	Welding parameters				Remarks
				Wavelength (nm)	**Power (W)**	**Spot size (cm2)**	**Exposure time (s)**	
Stewart *et al.* [70]	Vascular	IR diode	BSA solution w/ heparin	808	0.08	0.02	0.5	Microvessel thromboses were diminished w/low concentrations of heparin
Ott *et al.* [58]	Vascular	IR diode	BSA w/hyaluronic acid, ICG and sterilised water	808	0.41	0.1-0.27	30	Lower operative time and simplified procedure. Good results with 11 out of 14 welds successful.
					0.55		45	
O'Neill *et al.* [59]	Vascular	PTB w/ Nd:YAG	0.1% Rose Bengal solution	532	0.35	1	300	Absence of aneurism formation, Effective method for microvascular repairs without photothermal interactions.
Jonge *et al.* [37]	Vascular	CO_2	Deionised water w/ 25% BSA	10,600	0.17	0.012	261±40	Increase in welding strength and reduction in thermal damage.
Bogni *et al.* [36]	Vascular	IR diode	Polymer scaffold w/ 40% BSA solution and ICG	808	NR	0.21	NR	High-power, highly absorbing solder and a pulsed irradiation are preferred.
Pabittei *et al.* [67]	Vascular	IR diode Single-spot	Semi-solid BSA solution	670	1.6	1.3	50	Reduction of solder leakage. Adhesive bonding improved with single-spot technique.
		IR diode Scanning				0.27	82	
Pabittei *et al.* [57]	Vascular	IR diode	PCL scaffold w/ 48% BSA solution	670	0.096	0.08	25	Higher bursts strengths with PLGA over PCL. PLGA with better heat stability over PCL due to higher melting temperature.
			PLGA scaffold w/ 48% BSA and genipin solution					
Nakadate *et al.* [56]	Vascular	IR diode	NR	970	2.4	0.01	30	Preloaded longitudinal compression improves strength of LAVR procedure with good bursting pressures.
Bhatt *et al.* [23]	Vascular	CO_2	NR	10,600	0.1	NR	1	KTP with better functional recovery results (92.4%) over CO_2 (86.8%). KTP considered as a novel alternative to microsuture repair.
		KTP	NR	532	3-4	NR	1	
Hiebl *et al.* [71]	Vascular	IR diode	Polymer membrane w/BSA solution and ICG	808	0.25-1.5	NR	30	Improved solder allocation and cohesive strengths between solder and tissue.

NR. – Non referred.

3.2. Alternative techniques to laser welding technique

Besides the welding parameters and the use of solder solutions, the welding process is also influenced by other issues. Specifically, handling laser welding technique in three-dimensional approaches requires specific surgical skills due to necessary manipulation of vascular and nervous elements, which may lead to injury aggravation and procedure repetition [23,58]. To avoid manual surgical manipulation in the laser welding procedure, Ott *et al.* [58] presented an innovative surgical approach where the insertion of a laser fibre implemented in a balloon catheter allowed a 360 degree laser irradiation over a two-layer soldering (solder application) technique, achieving eleven successful welds within the fourteen executed (**Fig. 7**). Recently, Pabittei *et al.* [57] also verified that a laser fibre which delivers a 360 degree laser irradiation could also diminish thermal damage.

Although laser welding improvements were achieved with solder solutions, laser-activated dyes and an intraluminal device with 360 degree laser irradiation, inherent procedure thermal damage is still present with the application of such techniques. As an alternative to laser welding, photochemical tissue bonding (PTB) does not inflict any thermal damage to the welded and surrounding tissues. With this technique, sealing of tissue is achieved through the use of dyes that are chemically activated, such as Rose Bengal (RB) dye and Riboflavin-5-Phosphate, allowing the formation of fibre cross-linking bindings [60,61]. Results showed no operative and post-operative bleeding, absence of aneurysms, high tensile strength and the most important advantage over laser welding: no thermal damage. Due to the achieved results, the evolution of tissue repairs may be focused in innovative techniques associated with photochemical processes. [39,57,59,61,64].

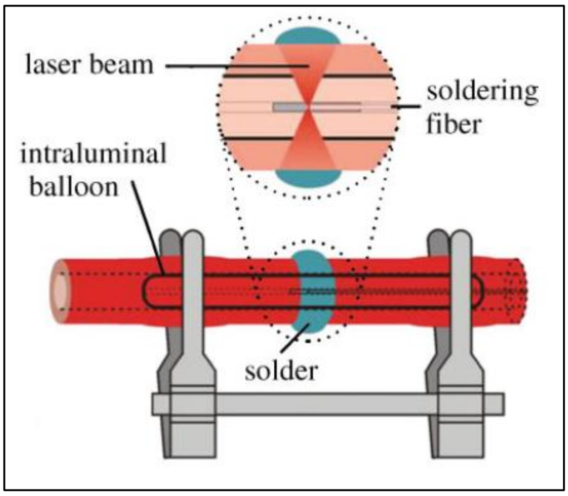


Fig. 7- Schematic of the laser-assisted vessel soldering [58].

In a completely different approach to vascular and nervous repairs, the application of high frequency electrosurgical welding (HFEW) technology as an alternative technique to laser photothermal and photochemical mechanisms was, in fact, successful and superior to sutured techniques. Korsak and Chaikovskii [30] presented an animal study where peripheral nerve repairs were made by welding soft tissues with high frequency current. The results showed similar morphology between sutured and high frequency welded nerves, with beneficial effects of HFEW in terms of the regeneration process.

Important progresses have been registered in laser welding of nervous and vascular tissues. However, new research directions are starting to emerge within these surgical practices. Auxiliary technological devices and instrumentation, such as robotic-assisted surgeries with enhanced image-processing systems [72–74], as well as the development of new biomaterials based on nanotechnology [75,76], show a great potential for driving the future evolution of reconstructive vascular and nervous laser welding.

3.3. Main remarks

- The application of laser welding techniques, in vascular and nervous repairs, is, presently, a common practice in the surgical field due to progressive and extensive studies in this field, over the last 40 years.
- Although laser welding has advantageous results, presenting non-foreign body reactions, absence of aneurysms, optimal tensile strengths and minimal associated thermal damage, additional sutures are still applied as a support guarantee of the procedure success.
- Thermal damage in laser welding techniques, despite being minimised, is still a concern in terms of the regeneration process. Different solutions can intercede to diminish thermal degeneration such as saline solutions or thermal controlled feedback systems.
- The bonding strength of vascular and nerve welds can be enhanced with the application of solder solutions, bonding materials and laser-activated dyes. Examples of these enhancements are albumin-based solder solutions, polymer scaffolds and ICG dyes, respectively.
- Alternative techniques for vascular and nervous repairs are a possibility, with demonstrated beneficial results. Techniques such as an intraluminal laser light source and the utilisation of photochemical dyes (PTB) to overcome nerve surgical manipulation and achieve non thermal degeneration, are of great importance to the innovation and development of new surgical procedures.

4. OTOLARYNGOLOGY

Through the conducted research, welding technologies were also present in the otolaryngology field, more specifically in tonsillectomy surgeries. The need for tonsillectomy surgery is identified through several symptoms which, in the majority of cases, are amygdala hypertrophy, chronic tonsillitis, peritonsillar abscess and obstructive sleep apnea syndrome [77–80]. These symptoms require tonsils removal or partial removal which results in the distinction between tonsillectomy (TE) and tonsillotomy (TO) procedures, respectively. The commonly surgical technique to perform both procedures is cold dissection, presented in 1909 [33,81]. However, the need for the improvement of surgical operation parameters lead to the research and experimentation of new techniques and devices with the purpose of characterising the most suitable for TE and TO surgeries. Since Mclaughlin surgical procedure with diathermy electrocoagulation in 1935 [82], the evolution of TE procedures allowed the application of various techniques recurring to electric, laser, plasma, ultrasonic and induced thermal power sources. Achieving excellent results towards bloodless, shortened and improved recovery surgeries, these innovative techniques were definitely beneficial for the medical and technological field. **Fig. 8** presents a chronological evolution, based on data from Verma *et al.* [81] and Slouka *et al.* [83] studies, towards the introduction of the thermal welding system by Karatzias et al. [77], in 2005.

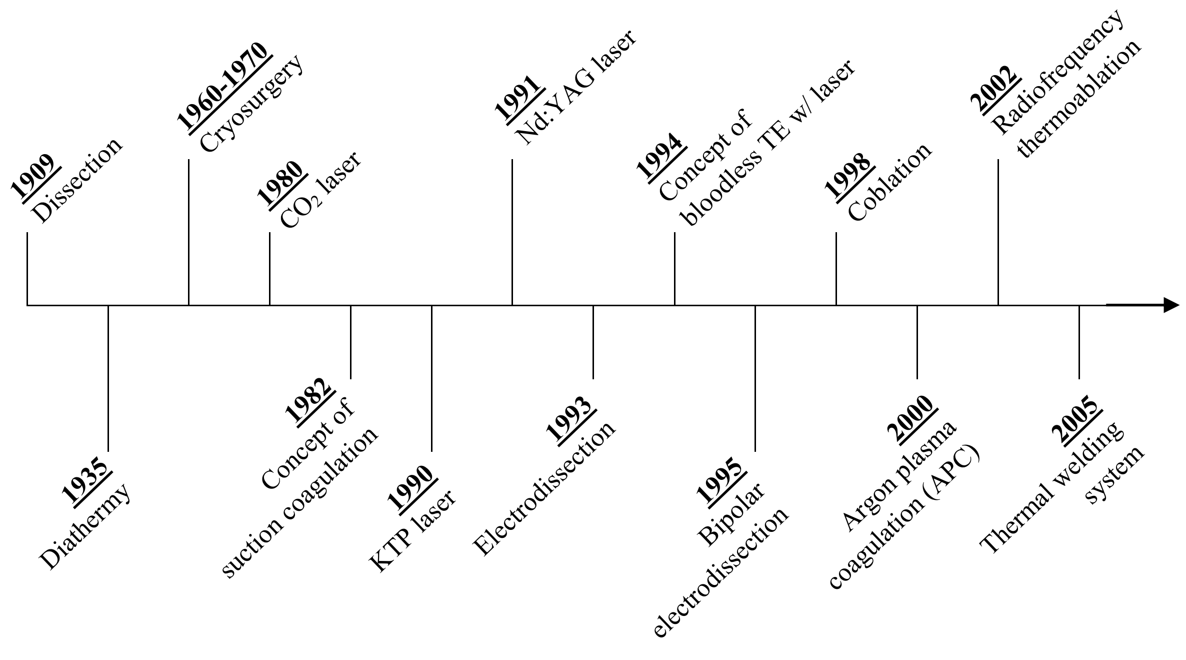


Fig. 8 - Chronologic evolution of TE techniques until 2005 (built based on data from [77,81,83]).

In the last 14 years, comparison studies focus their objectives in operative and post-operative results such as patient pain scores, bleeding rates, narcotic requirements and operation time [84–87].

According to literature, there is still no technique for TE or TO procedures that will assure optimal results when compared to the multitude of techniques already developed [81,83,88,89]. Even so, the present chapter focuses on thermal welding tonsillectomy (TWT), its instrumentation devices, advantages, drawbacks and achievements in TE surgery. Considering the conducted research, possibility of laser applications in this field is suitable but differs from thermal welding, which turns relevant the distinction between laser TE results and TWT results.

4.1. Techniques and instrumentation

As seen through the chronological evolution in **Fig. 8**, the variety of possible techniques implies the development of innovative surgical instrumentation devices. The standard cold dissection (CD) technique is applied through a tonsil knife or surgical scissors, a snare wire and hemostasis suturing [88–91]. Álvarez Palacios *et al.* [89] utilized absorbable sutures, previously analysed in vascular and nervous repairs (**Table 3 -** Techniques for nerve, arteries and veins repairs.), to achieve hemostasis in TE procedures. In terms of electrical energy, monopolar and bipolar electrocautery dissections (MCD and BCD, respectively) create an electric arc between the device and the surgical area which removes tonsillar tissue [86,91,92]. Alternatively to MCD and BCD, ligasure tonsillectomy uses the ligasure vessel sealing system (LVSS) which is a bipolar electrosurgical device with a scissor handpiece that grasp and seal vessels [93]. This device has an advantageous characteristic: a controlled energy delivery directly related with tissue density, reducing associated thermal damage of surrounding tissues [91]. Application of radiofrequency energy in tonsil procedures occurs in the radiofrequency and controlled ablation with non-heat driven soft tissue disruption (coblation) techniques. In the first, monopolar radiofrequency energy is conducted by inserting the probe into the tonsil tissue [81,83,85]. On the other hand, coblation devices apply radiofrequency energy in a plasma field, producing less thermal damage due to lower temperature ranges from 40ºC to 70ºC [94]. Similar to coblation, argon plasma coagulation (APC) utilises electrically ionised conductive argon to coagulate (plasma coagulation) and dissect tissue [44].

Considering the different techniques and their characteristics, **Table 10** exposes an overview of these instrumentation devices and types of energy, linked with TE and TO surgeries.

Table 10 - Overview of TE/TO techniques and instrumentation.

Study	Technique	Energy	Instrumentation
Veerakumar *et al.* [90]	CD	Mechanical	Tonsil knife/scissors, snare wire and sutures
Chimona *et al.*[85]	Radiofrequency	Radiofrequency	Sutter BM-78911 Radiofrequency unit w/ To-BiTE^{TM} clamp
Karatzanis *et al.* [93]	Ligasure	Electrical	LVSS w/ LS1200 Ligasure Precise
Özkırış [86]	BCD	Electrical	Statome 900 Diathermy machine w/ bipolar forceps
Karatzias *et al.*[84]			Karlstorz bipolar coagulator w/ Bayonet bipolar forceps
Álvarez Palacios *et al.* [89]	MCD	Electrical	Monopolar diathermy machine
Silvola *et al.* [95]			Erbotom 450
Elbadawey *et al.* [94]	Coblation	Bipolar radiofrequency	Coblator II system w/ Evac T&A plasma wand
	Diode Laser	Laser	Ceralas^{TM} D25 (980 nm) w/ Endostat fibre optic (0.6mm)
Papaspyrou *et al.* [44]	APC	Plasma	Monopolar argon supported needle
Lourijsen *et al.* [43]	CO$_2$ Laser	Laser	F125 laser tube (beam diameter 3 mm)

When thermal welding tonsillectomy is applied, the Starion system device is normally utilised. It is a system constituted by a universally power supply (UPS), a footswitch and a handpiece which, commonly, is the LS1200 Ligasure Precise (TLS^2) or the Ultraslim Bayonet forceps (**Fig. 9** and **Fig. 10**, respectively) [31,77,93,96]. In both handpieces, a nichrome heating element is activated through the compression of the forceps and is also controlled by the footswitch, meaning that thermal energy is produced with a resistant heating wire actuated by low voltage direct current [33,80,85]. It is important to keep in mind that despite the UPS device, no electric current reaches tonsil tissue due to the thermally insulating backing of the nichrome element which protects heat dissipation along the handpiece (**Fig. 11**). The difference between TLS^2 and Ultraslim Bayonet forceps is that TLS^2 permits a better surgery visualization and has a 360º rotational handling [93,96]. Accordingly to the majority of TWT studies, standard power settings for this system are “1” and “8” for coagulation and dissection of tonsil removal, respectively. However, Celebi *et al.* [87] and Özkiriş *et al.* [88] demonstrated that with power settings of “2” to “4”, coagulation and sealing are also possible.

Fig. 9 - The LS1200 Ligasure Precise handpiece [31].

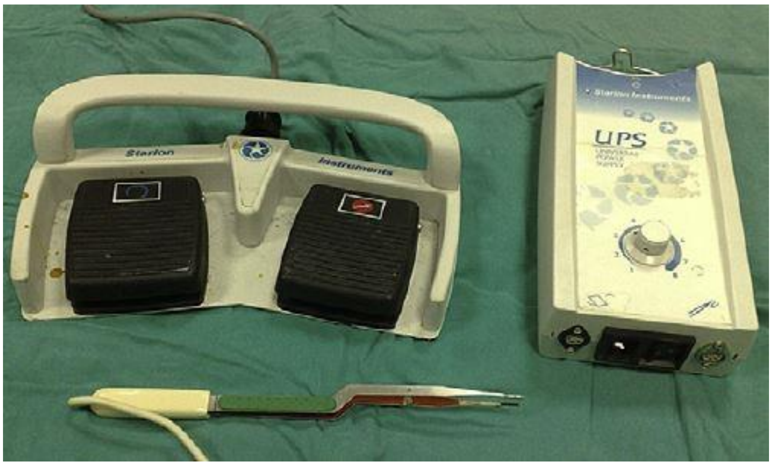


Fig. 10 - The Starion Thermal Welding System [93].

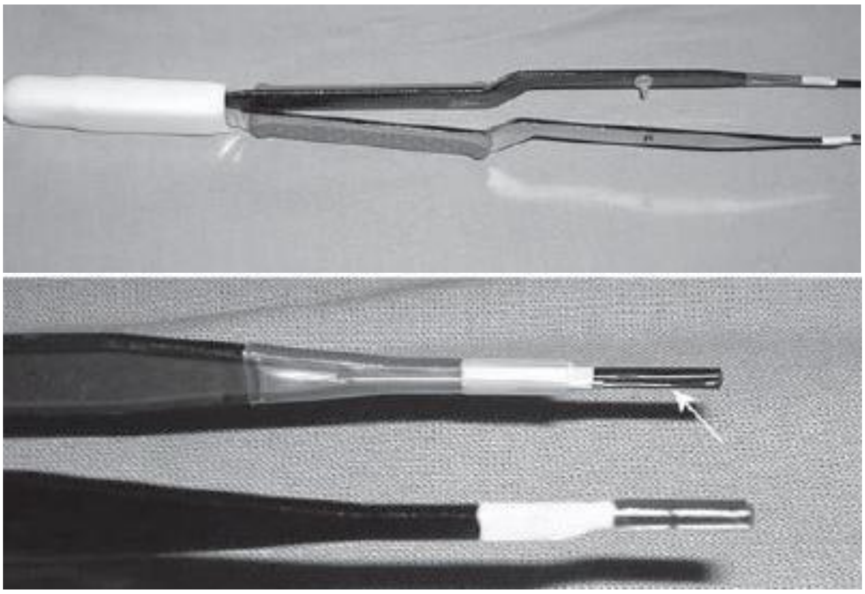


Fig. 11 - The tip of the Bayonet Ultraslim Forceps. The active part of the instrument is composed of a nichrome heating element (white arrow) with a thermally insulating backing [77].

With this new TWT surgical instrumentation, one of the advantages is that reusable instruments are no longer applicable and so the operation is carried with disposable forceps. Since bovine spongiform encephalopathy (BSE) prions are resistant to standard sterilisation methods, reusable instruments have, according to Sayin and Cingi [91], potential risk of transmitting prion infections from one patient to the other. With disposable instruments, the risk of dissemination of variant Creutzfeldt-Jakob disease (vCJD) is prevented [77,87,88,96]. Consequently, the single used instruments increase the total cost of the operation which can lead medical institutions to consider the application of other techniques instead of thermal welding tonsillectomy [84,87].

From literature research it was verified that the cost-overview[1] for TWT instrumentation range from, approximately, 148€ to 400€ (**Fig. 12**). In Cunningham and Chio [92] cost analysis, between electrocautery (EC) and TWT, it was concluded that TWT was too expensive, with an instrumentation cost increase from 12€, in EC technique, to 148€ with thermal welding. Other literature also indicates that TWT is an expensive technique compared to other techniques such as CD, BCD or radiofrequency [85,86,88]. However, medical institutions should carefully analyse the benefit-cost of TWT instrumentation before excluding its application. Approaching TWT technique has a medical investment to the institution and to the patient’s safety and recovery, can be an advantageous optimisation for TE surgery practice, since thermal welding surgery offers proved beneficial operative and post-operative results with the addition of diminishing the risk of possible infections.

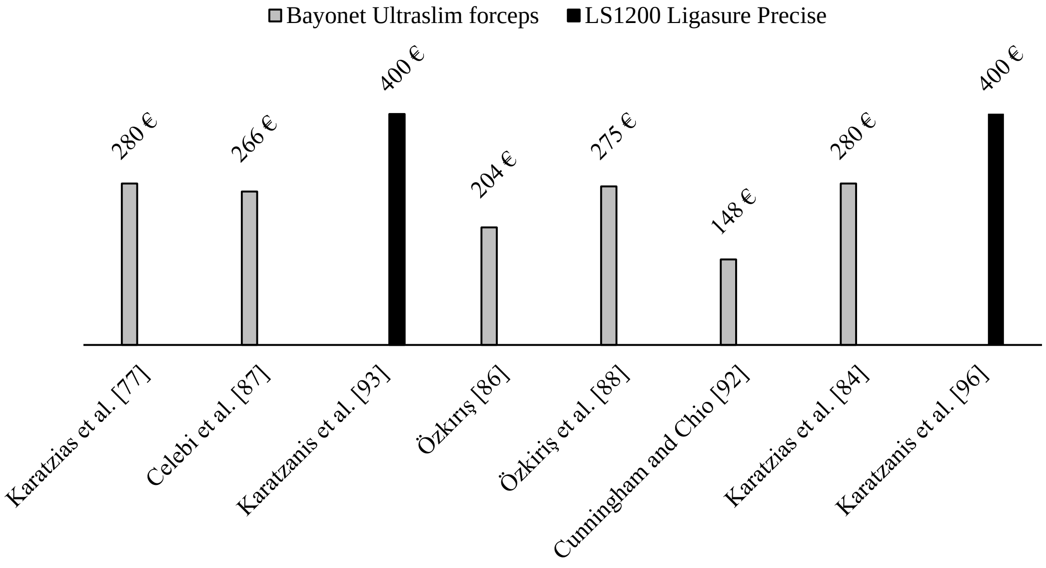


Fig. 12 - Cost overview of Bayonet Ultraslim forceps and LS1200 Ligasure Precise.

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[1] In order to present currency coherence, this cost-overview is presented in euros (€).

4.2. Thermal welding tonsillectomy

As mentioned early, in TWT, no electric current reaches tonsil tissue due to the thermally insulating backing of the nichrome element in the forceps tip. Thus the results of TWT instrumentation are efficiently achieved with direct thermal energy application [86,93]. According to literature [84,95], the procedure is divided in two phases: coagulation (sealing) and dissection (**Fig. 13**).

Fig. 13 - Tonsillectomy procedure [96].

The first phase occurs when the heat produced between the two tips of the instrument increases and cellular protein denaturation initiates, with protein molecules adhering to one another as higher focal thermal energy is achieved [31,86,88,93]. This denaturation process modifies the mechanical elastic properties derived from tissue shrinkage, containing collagen fibers with a Young's modulus of 1 MPa, and so tissue thermal strain is verified [97]. Subsequently, a graded thermal profile is generated and the second phase takes place with tissue dissection occurring under the effect of forceps pressure and at a temperature range of 300-400ºC (**Fig. 14 – Tissue detachment zone**). From distances greater than 500 microns of the thermal focal point (TFP) center, vessel sealing occurs due to lower temperatures between 60-100ºC (**Fig. 14 – Coagulation zone**) [33,80,98].

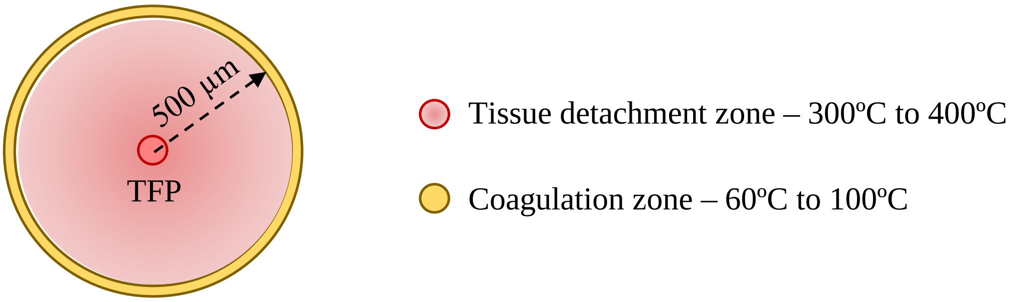


Fig. 14 - Tissue thermal profile in TWT technique.

Additionally, the epicenter of this graded thermal profile contains most of the heat thus thermal damage to peripheral tissues is reduced. Due to this mechanical and thermal intervention, inflammation, contractions of pharyngeal muscles and nerve damage occurs, and so post-morbidity evaluation in TWT surgeries is of great importance to understand the effects and improvements achieved with this technique [87,99].

4.2.1. Operative and post-morbidity parameters

Surgical parameters such as operative-time, post-operative pain, narcotic requirements, intra and post-operative bleeding are the most common when evaluating TE surgery's success. In TO surgeries, intraoperative blood loss and post-operative pain are lower than in TE due to no intervention in the peritonsillar tissue, which contains blood vessels and nerve fibres, during the dissection procedure [43,44].

In most literature, the comparison of TWT technique with cold dissection results in beneficial outcomes, commonly in three of the mentioned parameters: operative-time, intraoperative bleeding and post-operative pain. When observing operative-time related results, TWT is a less time consuming technique due to both surgery phases being executed with the same instrument which excludes the need to change device between coagulation and dissection procedures [87]. The same results cannot be verified in **Fig. 15** where TWT is compared with other techniques such as MCD, BCD, ligasure TE or radiofrequency. Although surgical time is slightly superior to the techniques mentioned, authors argument that the differences are not statistically significant and therefore, the applicability of thermal welding in TE surgery is considered suitable.

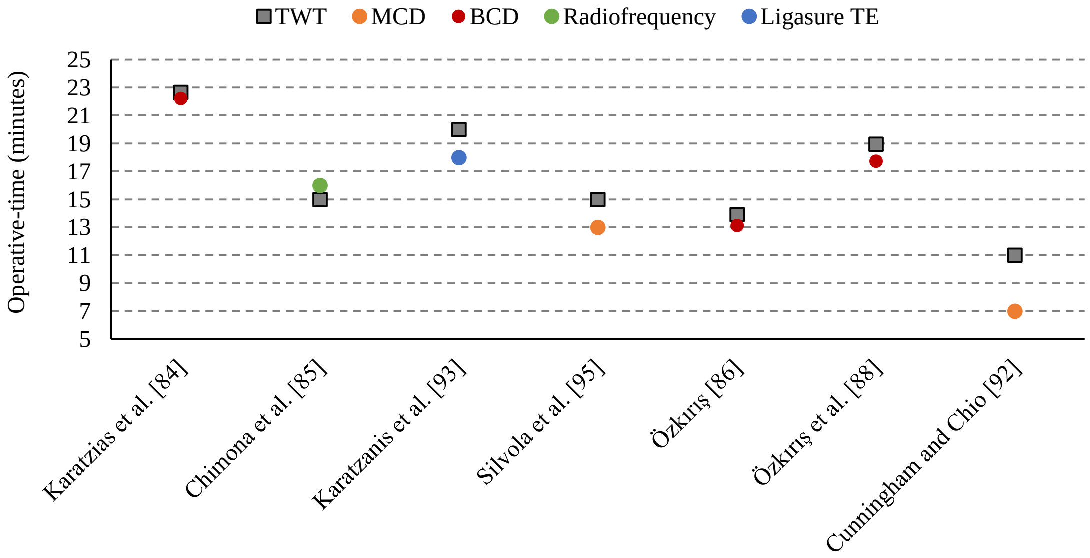


Fig. 15 – Comparison of operative time results between TWT and MCD, BCD, radiofrequency and ligasure TE.

Cross-linking intraoperative bleeding results from comparison studies between TWT and CD, it is noticed that, in the majority of cases, they are beneficial and also that, in some, it does not occur [79,86,95]. This is only possible if the coagulation of tonsil tissue is achieved correctly, accordingly to the process of denaturation described in the first phase of the TWT procedure. For example, Özkiriş *et al.* [88], by applying TWT, reduced intraoperative blood loss from 38.08 ± 10.83 ml (CD) to 10.13 ± 4.14 ml and positive results were also obtained by Karatzanis *et al.* [96], Yilmaz *et al.* [31] and Celebi *et al.* [87] presenting no intraoperative bleeding results. In this matter, comparison with the same techniques mentioned in the surgical-time approach, show that TWT might be an advantageous technique. Observing the values exposed in **Fig. 16**, there is not a consistent replicability that can assure an advantageous outcome of TWT when compared to BCD, for example. However, this analysis does not indicate that TWT applicability is not viable. Similar to surgical-time parameter, the deviances in intraoperative bleeding are not statistically significant, according to the authors mentioned in **Fig. 16**.

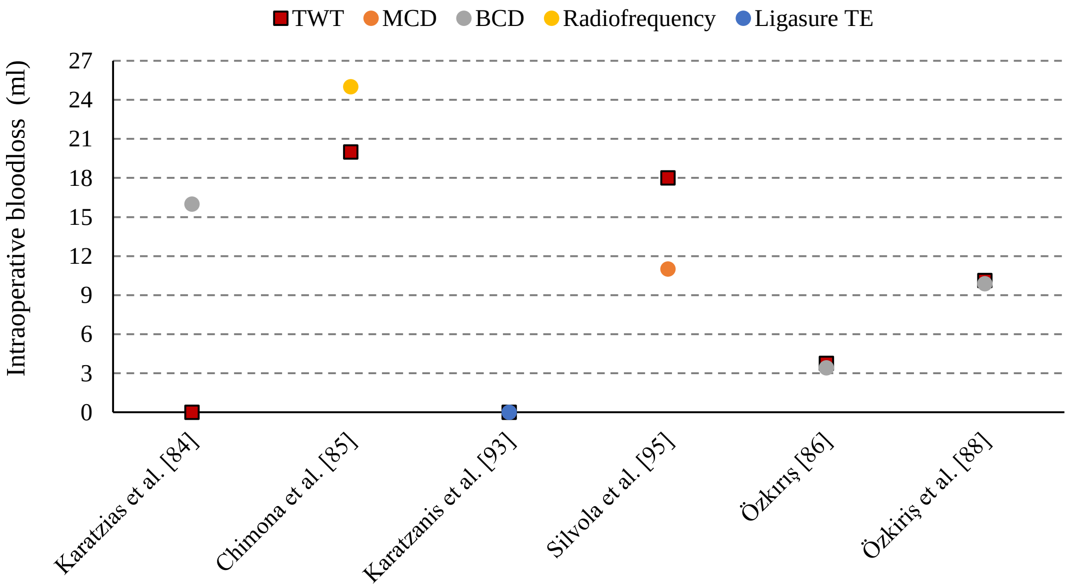


Fig. 16 - Comparison of intraoperative bleeding results between TWT and MCD, BCD, radiofrequency and ligasure TE.

Post-operative pain can be assessed by a visual analogue scale (VAS) or by a pain score evaluation from zero (no pain) to ten (excessive pain) [31,98]. Thermal welding tonsillectomy also intercedes in this field with confirmed advantageous outcomes. Evaluating the pain scores, through the conducted research, TWT presents significantly improved results when faced by other TE techniques such as CD, MCD, BCD, radiofrequency or ligasure TE (**Fig. 17**). Additionally, Michel *et al.* [78] reduced pain scores by 61.9% with TWT application against harmonic scalpel and electrocautery method. It is also important to refer that minimisation of associated thermal damage can, effectively, influence patient pain sensibility and recovery. Karaca *et al.* [99] demonstrated a significant reduction in post-operative pain by cooling down the tonsillar fossae during surgery, improving the healing process with healing grades between 75% and 100%.

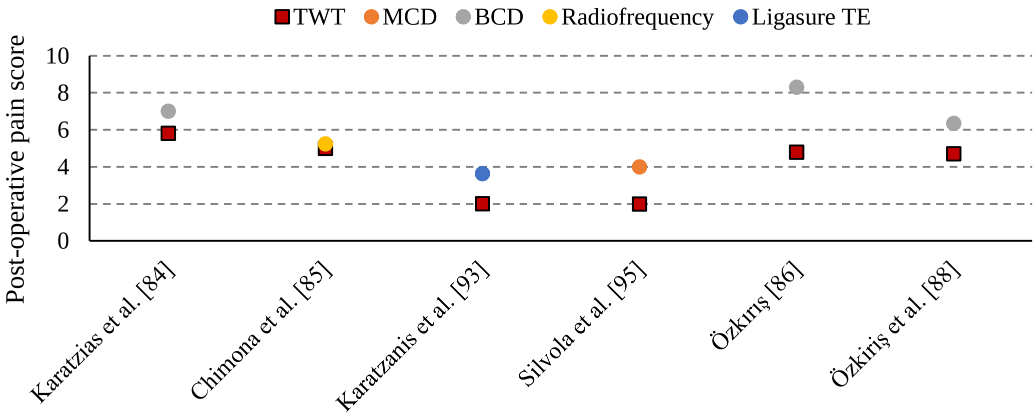


Fig. 17 - Comparison of post-operative pain results between TWT and MCD, BCD, radiofrequency and ligasure TE.

The continuous research, over the last 14 years, in the field of thermal welding tonsillectomy, led to the development, evolution and acceptance of its implementation as a viable surgery method when it comes to TE surgery. TWT revealed to be a safe, efficient and a post-morbidity enhancement relatively to other tonsillectomy surgical methods applied but it is still necessary to continue researching and improving this medical procedure with the development of innovative instrumentation and performance, towards a less invasive, more efficient and reduced patient post-morbidity procedure.

4.3. Non-thermal laser techniques

Contrary to vascular and nerve laser repairs, bibliographic literature differentiates laser application in otorhinolaryngology surgeries since it does not imply a direct correlation with the thermal welding procedure. Laser interactions in this medical field are mainly for the treatment of malignant and benign laryngeal diseases, excision of tumors in the oral cavity, ablation of subglottic hemangiomas and also including tonsils partial or total removal [90,94,100]. Laser-tissue mechanisms can be achieved with photothermal and photochemical reactions, as seen in the previous chapter (**3.2 - Alternative techniques to laser welding technique**) with the alternative method for nerve repair, photochemical tissue bonding. Therefore, **Fig. 18** demonstrates the different mechanisms for laser-tissue interactions used in the mentioned treatments, considering the delivered power density and time of exposure [97].

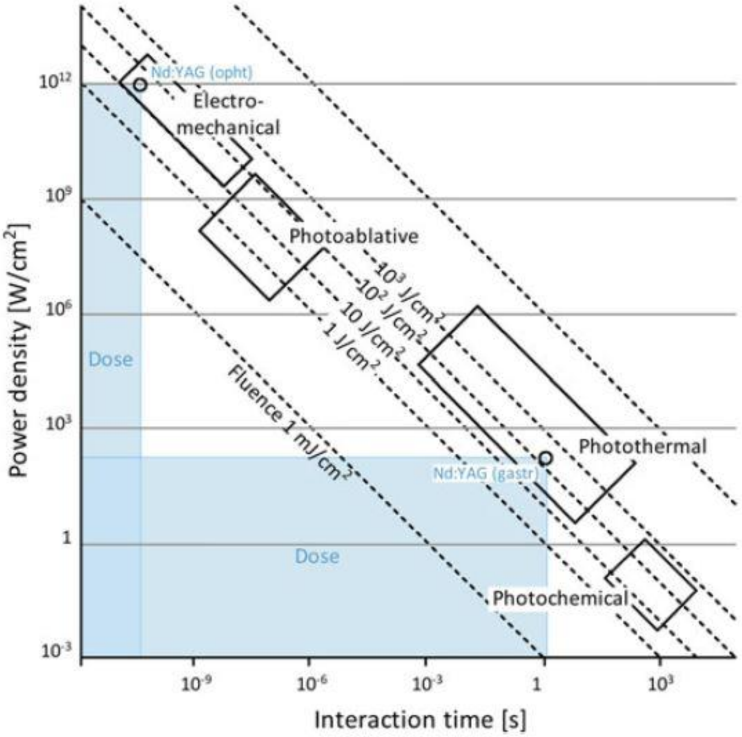


Fig. 18 - Medical laser interaction map. The diagonals show several lines of constant fluency (J/cm^2) [97].

The TE coagulation and dissection phases are still verified, with the particular difference of photon distribution being dependent of tissue biological properties and their compatibility with laser wavelengths. Thus, accordingly to Rothholtz and Wong [100], with different wavelengths and delivery methods, laser application in otolaryngology surgeries will also differ as demonstrated in **Table 11**. Observing the laser types exposed, it is of notice that CO_2 laser is suitable with the tonsillectomy and tonsillotomy procedures. Other authors such as Elbadawey *et al.* [94], Papaspyrou *et al.* [44] and Verma *et al.* [81] also confirmed that CO_2 laser TO can achieve beneficial intraoperative bleeding and post-operative pain results. Alternatively to CO_2 laser application, Papaspyrou *et al.* [44] also applies an interesting technique: argon plasma coagulation (APC). In this technique, selectively superficial thermal tissue destruction is induced, with limited depth penetration of 1 to 2 mm. Furthermore, the absence of tissue carbonisation is an advantageous histological benefit along with the non-required surgical specialisation in APC procedure. In terms of advantages of laser applications in TE/TO surgeries, less intraoperative blood loss and post-operative pain is verified. However, most of them require excessive surgical time (when compared to CD), high investments and have a learning curve associated [90]. An example of these drawbacks is Slouka *et al.* [83] study, where Ho:YAG and Er,Cr:YSGG diode lasers were compared, concluding that the results did not showed to be significant towards a cost-benefit leverage, and so CD was still the most suitable choice for the procedure.

Table 11 - Laser applications in otolaryngology [100].

Laser type	Wave length	Penetration depth	Delivery methods	Indications/applications
Argon	514 nm	0.8 mm	Fibre Micromanipulator Focusing handpiece	Ear – Stapes surgery Nose - Telangiectasias
CO_2	10,600 nm	30 µm	Articulated arm Micromanipulator hollow wave-guide scanner Focusing handpiece	Glottis/subglottis/larynx/ oropharynx Benin/malignant Therapeutic/diagnostic Tonsils Lingual Oral cavity/tongue Benin/malignant Therapeutic/diagnostic Nose Turbinate hypertrophy
Erbium:YAG	2,940 nm	3 µm	Articulated arm sapphire fibre	Nose Rhinophyma Cosmetic Laser resurfacing
Holmium:YAG	2,120 nm	0.4 mm	Fibre/bare fibre contact Handpiece	Nose Sinus surgery Turbinate hypertrophy
KTP	532 nm	0.9 mm	Fibre/bare fibre contact Side-fire Focusing handpiece Diffuser tip Micromanipulator	Nose Polyps Epistaxis Oropharynx/palatine tonsils Obstructive sleep apnea Vascular malformations Nose Telangiectasias Trachea Stenosis Subglottic haemangioma
Nd:YAG	1,064 nm	4 mm	Fibre/bare fibre Contact tips	Vascular malformations Tumour removal (contact mode) Turbinate surgery

4.4. Main remarks

- Different techniques have been applied in tonsil surgeries since the introduction of cold dissection. From radiofrequency, electrocautery, plasma coagulation and laser, thermal welding technology allowed an overall improvement in operative and post-morbidity results such as pain scores, operative-time, narcotic usage and post-operative bleeding.
- Surgical instrumentation of TWT does not require the utilisation of reusable instruments which consequently reduces the risk of a variant Creutzfeldt-Jakob disease dissemination. However, there are still medical institutions that do not choose TWT to perform tonsillectomy surgery due to cost-benefit evaluations.
- TWT technique is performed in two phases (coagulation and dissection), both can be executed with the same instrument which benefits this technique with lower surgical times. According to literature research, the differences exposed in post-morbidity results are not statistically significant to compromise TWT as a viable technique for tonsil surgery.
- Laser application in tonsillectomy and tonsillotomy surgeries, is also a possible and viable solution, although it requires higher costs, surgical experience and presents excessive operative times.
- From the multitude of lasers utilised in otolaryngology, CO_2 laser is the most suitable for tonsils partial or total removal. In this matter, argon plasma coagulation technique proved to be an alternative approach with beneficial results.
- Regardless of no consensus in the medical and scientific communities for an optimal technique, in general, TWT is an efficient and safe tonsillectomy method with proved beneficial results when compared to cold knife dissection and other existing technologies. However, further improvement in innovative instrumentation devices for this technology is necessary to surpass the cost-benefit drawback that is still a concern for medical institutions.

5. OPHTHALMOLOGY

In early years, conventional incisions and closures of eye surgeries with sutures were reliable and inexpensive procedures[40,101]. However, it was noticed that their application implied foreign body reactions, prolonged operative time, high technical experience and promoted post-operative complications such as corneal astigmatism, tissue inflammation, wound leakage and irritation of the conjunctiva [102–105]. The present chapter exposes the laser intervention in ophthalmic surgery since the development of the xenon-arc photocoagulator by Meyer-Schwickerath, in 1956 [106,107]. Ophthalmic incisions with femtosecond lasers are briefly approached, although the intended focus being on the evolution and results of eye closure procedures with laser welding technologies.

With the innovation in the ophthalmology field, a precise observation of the anatomy of the human eye became possible through eye scanning. Accordingly to Krauss and Puliafito [107], the application of diagnostic lasers made possible the reproduction of retina images through the scanning laser ophthalmoscope (SLO). The creation of a pattern with retina measurements, retrieved three-dimensional images and ophthalmologists became able to clearly identify eye anomalies and to decide on the most effective and safest type of intervention.

Furthermore, ophthalmic laser applications were categorised in two groups [108], considering the range of different wavelengths available: (1) Visible or near-visible infrared laser wavelengths to treat retinal disease or glaucoma; (2) Nonvisible wavelengths for refractive surgery to reshape the cornea for vision correction. This wavelength distinction is directly related with the application of eye laser welding technologies, differentiating bladeless incisions with femtosecond lasers from thermal repairs with photocoagulation (**Fig. 19**).

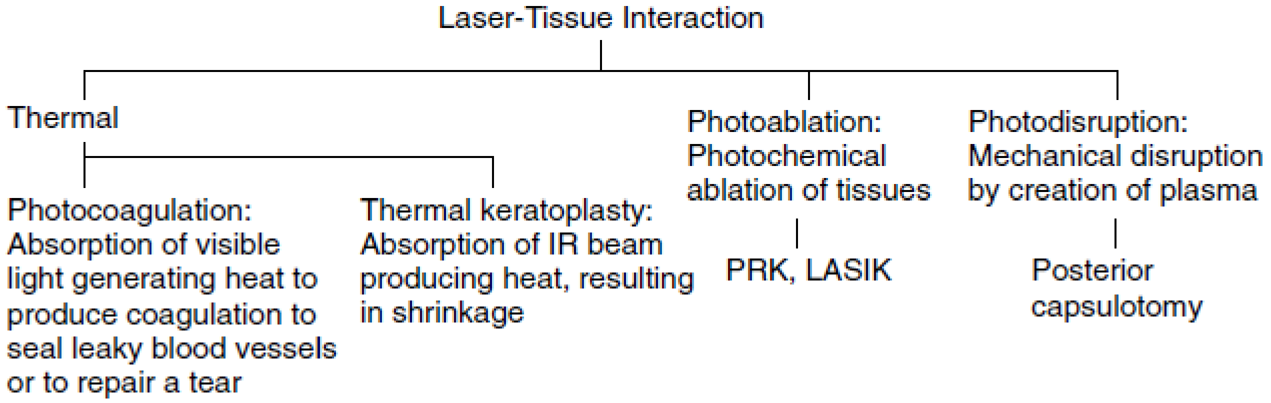


Fig. 19 - Various laser-tissue interaction mechanisms in ophthalmology [108].

5.1. Ocular laser-tissue interaction

In respect of femtosecond lasers, photodisruption occurs, i.e. the emission of light pulses of short duration promotes the disruption of tissue links [107]. These lasers have been implemented in a large range of eye surgeries (**Table 12**). For the particular case of deep anterior lamellar keratoplasty (DALK), Aristeidou *et al.* [109] refer that femtosecond lasers allowed the precise identification of tissue depth and air injection, promoting a more secure wound closure over the conventional manual techniques. However, they also report that the effects of femtosecond lasers in descement's stripping endophelial keratoplasty (DSEK) or cataract surgeries require more investigation and optimisation to be reliable.

Table 12 - Femtosecond application procedures [109].

Femtosecond application procedures	Laser in situ keratomileusis (LASIK)
	Small incision lenticule extraction (SMILE)
	Penetrating keratoplasty (PKP)
	Insertion of intracorneal ring segments
	Cataract surgery
	Deep anterior lamellar keratoplasty (DALK)
	Descement's stripping endophelial keratoplasty (DSEK)

From the previous **Fig. 19**, it is possible to observe that laser-tissue interaction mechanisms in ophthalmic surgeries can also be made with a thermal approach. Meyer-Schwickerath xenon-arc photocoagulator was the starting point to laser eye surgery evolution. With it, laser instruments evolved and selection of parameters such as exposure time, laser absorber, laser type and energy dosimetry, led to the optimisation of the photocoagulation procedure [63,67,71]. As aforementioned, the importance of the wavelength in laser optical surgery is of utmost significance since it is the absorption compatibility that allows successful photothermal tissue interactions [111]. In ophthalmic applications, it is necessary that laser light wavelengths traverse the ocular media without absorption or energy loss [112]. Zinn [112] characterises the retina and choroid structures according to their spectral ranges, therefore concluding that successful photocoagulation is obtained from 450 to 650 nm (**Fig. 20**).

Structure	Spectral ranges (nm)
Macular pigment	450-490
Retinal surface	450-500
Retinal nerve fibre layer	490-540
Retinal vessels	550-590
Choroidal vessels (superficial)	570-590
Retinal pigment epithelium	590-610
Choroidal vessels (deep)	620-650
Melanin	620-650

Fig. 20 – Light absorption by retina and choroid structures [112].

Parallel to the wavelength characterisation for ocular structures, laser-tissue interactions have also to be considered in the thermal modification behaviours of such structures. In this matter, Rossi *et al.* [113] identified four distinct structural modifications between 20ºC and 90ºC temperature range. With different reorganisation stages of the cornea collagen, different cross-linking welding strengths are achieved. Through the conducted research it is possible to verify that temperatures between 60ºC and 80ºC are the most adequate to a successful eye surgery with beneficial results [24,40,114,115]. Additionally to Rossi *et al.* [113] categorisation of heated structural collagen changes, laser tissue welding (LTW) can also be differentiated in soft, moderate or hard welds within the mentioned temperature range, according to Pavone [35]. **Fig. 21** illustrates the process of collagen transformation when subjected to different heating effects.

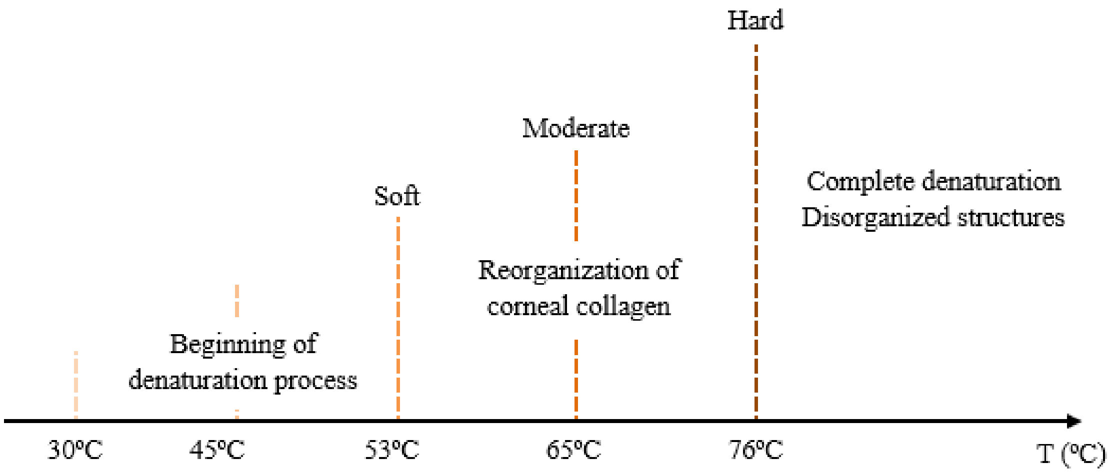


Fig. 21 - Collagen biological process with temperature increase.

From these laser-tissue interactions it is implied that thermal stability is the main goal for an appropriate welding. Proved to be an innovative technique with beneficial enhancements over suturing such as reduced intervention time and simplification of the procedure [103,115,116], ophthalmologists are still concern with one major drawback in its medical application: cornea thermal damage and its subsequently inflammation [40]. In these cases, coagulation of the cornea may occur and modify its curvature resulting in possible astigmatism [114].

5.2. Ophthalmic instrumentation

During the years of 1968 and 1969, breakthroughs in laser ophthalmic surgery were achieved with the development of the slit-lamp argon laser photocoagulator and with the first treated patient, respectively [106]. In this device, the laser light is conducted to a movable half-silvered mirror that reflects and aims the beam into the patient's eye. The possibility of varying the beam spot size is accomplished by adjusting the lens wheel, as illustrated in **Fig. 22** [112].

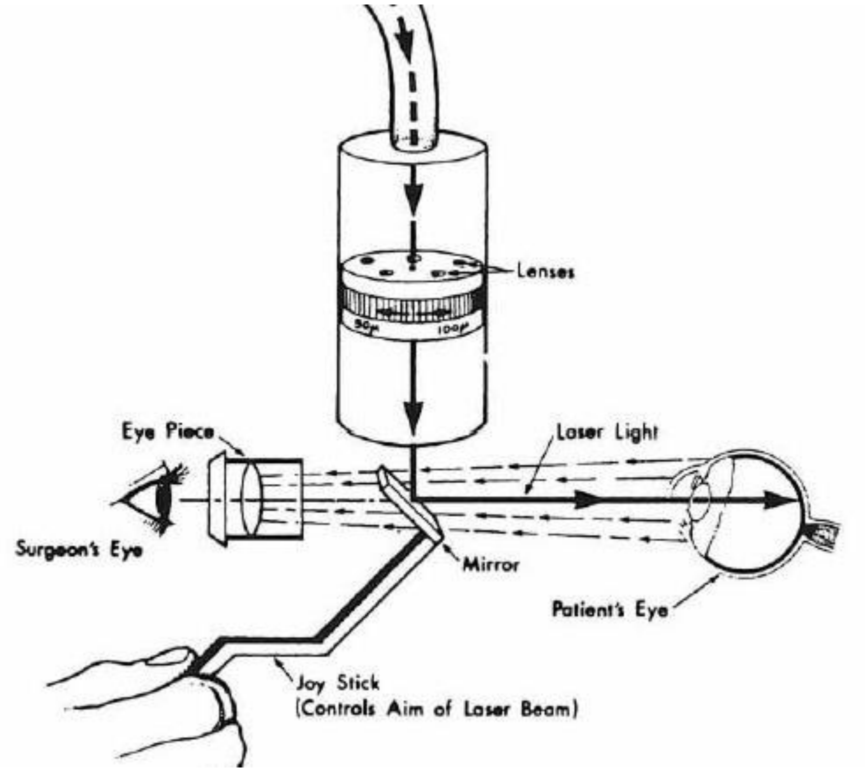


Fig. 22 - Schematic representation of the slit lamp argon laser photocoagulator [112].

Additionally, the beam spot size can also be altered in accordance to the type of lens utilised: plano, convex or concave. If the lens input dosimetry ratio is equal to all three types, then a convex lens will produce smaller spot sizes while increasing output dosimetry ratio. On the other hand, when concave lenses are applied, large spot sizes are produced and decrease in the lenses output dosimetry ratio will be noticed (**Fig. 23**). According to Zinn [112], for the utilisation of this argon laser photocoagulator, laser light intensity could not be modified through the fibre optic diameter hence the importance of the lens type.

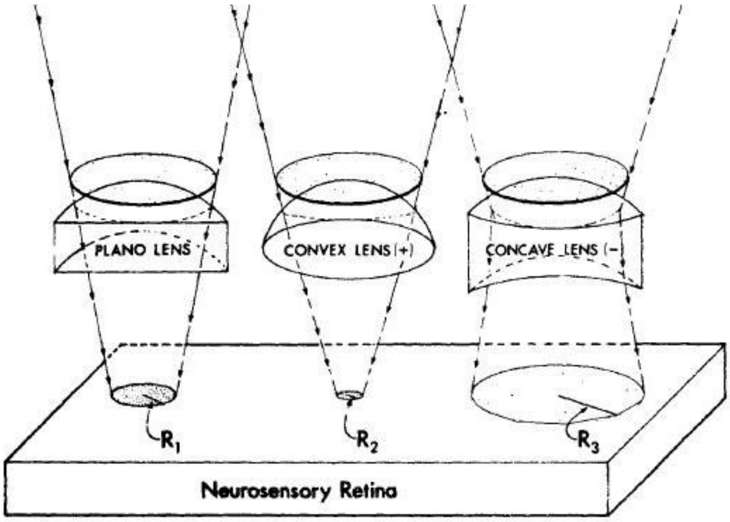


Fig. 23 - Schematic view of laser beams showing the lenses effect on the final size of the laser beam [112].

Nowadays, the instrumentation devices for ophthalmic surgeries are more sophisticated and surgery friendly, demonstrating significant improved results over the first devices developed 40 years ago. In 2014, Rossi *et al.* [117] presented a robotic console for ocular surgery consisting of a macro and micro-positioning system, proximity and pressure sensors and a stabilising tool, connecting the patient eye to the robotic arm (**Fig. 24**). With this device, defects of manual handling surgeries are eliminated and a better visualisation of the optic disc is allowed [117].

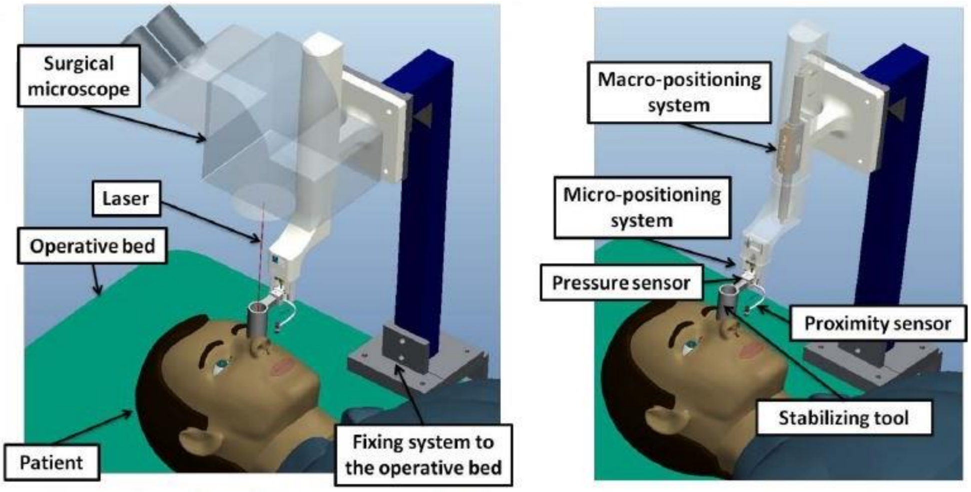


Fig. 24 - Robotic platform for laser assisted ophthalmic surgery [117].

In terms of ocular leakage and tensile strength measurements, pressure transducers (**Fig. 25a**) and digital force gauges (**Fig. 25b**) can be utilised combined with Seidel tests, which allow the identification of ocular leak sites after an ophthalmic surgery [115,118].

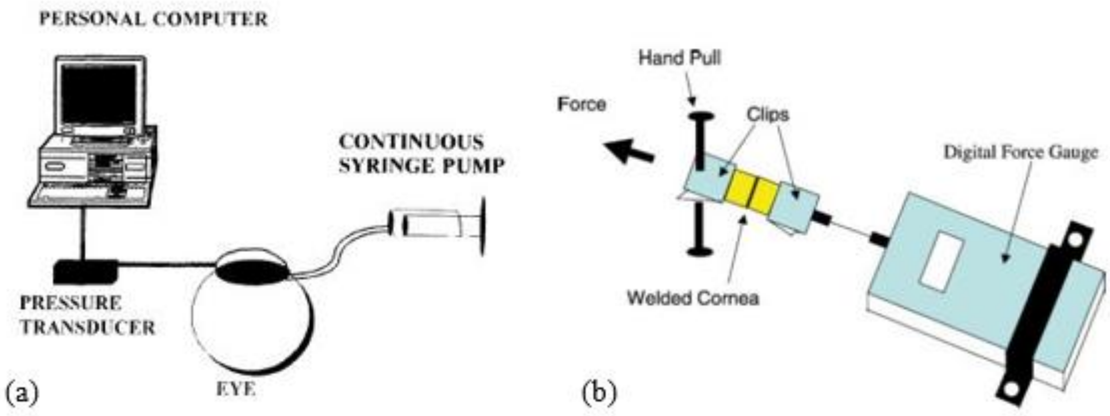


Fig. 25 - Instrumentation for ocular tensile strength measurements. (a) Pressure transducer system; (b) Digital force gauge [115, 118].

5.3. Laser welding technique

Laser welding of ocular tissues have similar approaches to those of vascular and nervous repairs (**3.1 - Laser welding technique**). The technique can be applied through direct welding, laser soldering and ultimately through dye-enhanced soldering [108,114]. This ophthalmic biological interaction with laser energy is translated by the reconstruction of collagen bindings through thermal modifications [116]. This reconstruction can also be used to promote the formation of intentional scars in ocular weak areas, repairing and strengthening retinal tears (**Fig. 26**).

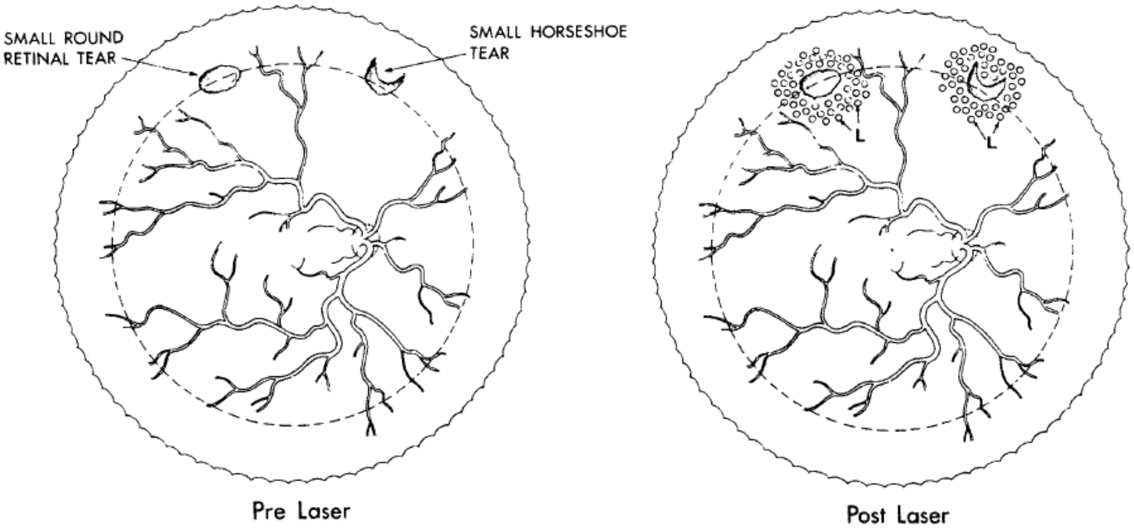


Fig. 26 - Argon laser photocoagulation therapy for peripheral retinal tears [112].

Laser technologies and welding procedures revolutionised ophthalmic practices in eye surgery. However, as illustrated in **Fig. 27**, a careful selection and control of the laser parameters, the thermal feedback systems and the type of solder is required. All these factors determine the success of ophthalmic laser welding surgery because they influence the tissue damage, the procedure safeness, and the tissue regenerative time.

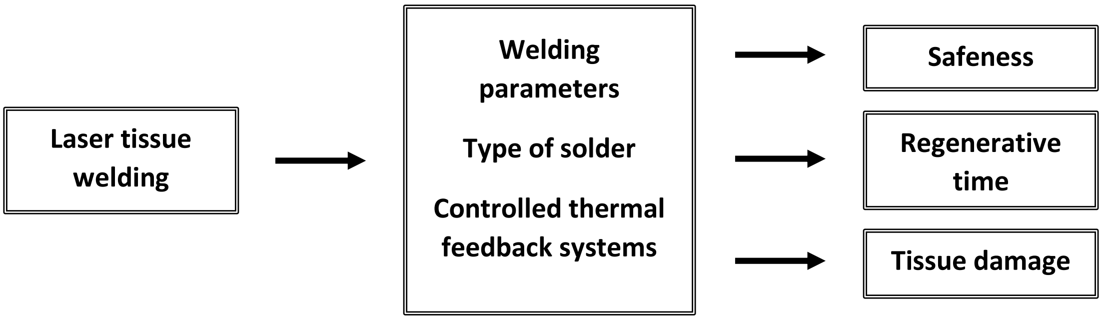


Fig. 27 - Laser welding principal factors and their influence on tissue damage, regenerative time, and safeness.

5.3.1. Thermal control and image-processing

To accurately control the operating surgical conditions, thermal-controlled feedback systems have been introduced in eye laser welding procedures. These systems control the temperature of the weld through a radiometer, two optical fibres and the computerisation of the recorded data (**Fig. 28**). The optical fibres are important elements due to their function of transmitting radiation. Thus, the materials chosen for such fibres have to be carefully analysed. According to Strassmann *et al.* [119], standard optical fibres are made of silica glasses, have highly transparent properties in the visible and near infrared (NIR) radiation with wavelengths inferior to 3 µm which are useful for Nd:YAG or GaAs radiation but when it comes to CO_2 laser emission, they are not suitable since CO_2 has a common wavelength of 10.6 µm (IR). In those cases, various authors [105,118,119] recommend the utilisation of polycrystalline silver halide optical fibres that are also highly transparent but actuate in the mid-IR, i.e. between wavelengths from 3 to 30 µm. These fibres have also advantageous properties such as flexibility, non-toxicity, non-soluble in water and are biocompatible [40,101].

In terms of process, the standard distinction of both optical fibres can be made with one inducing the laser beam into the ophthalmic tissue and the other guiding radiation to the thermal detector [101,118,119]. However, Gabay *et al.* [114] improved the concept of these systems by implementing only one optical fibre that could perform both functions, as illustrated in **Fig. 29**. To achieve this innovative concept, laser beam and blackbody frequencies had to be synchronised to allow the utilisation of the same fibre without any cross information. Gabay *et al* [114] concluded that this system is advantageous over the two-fibre system.

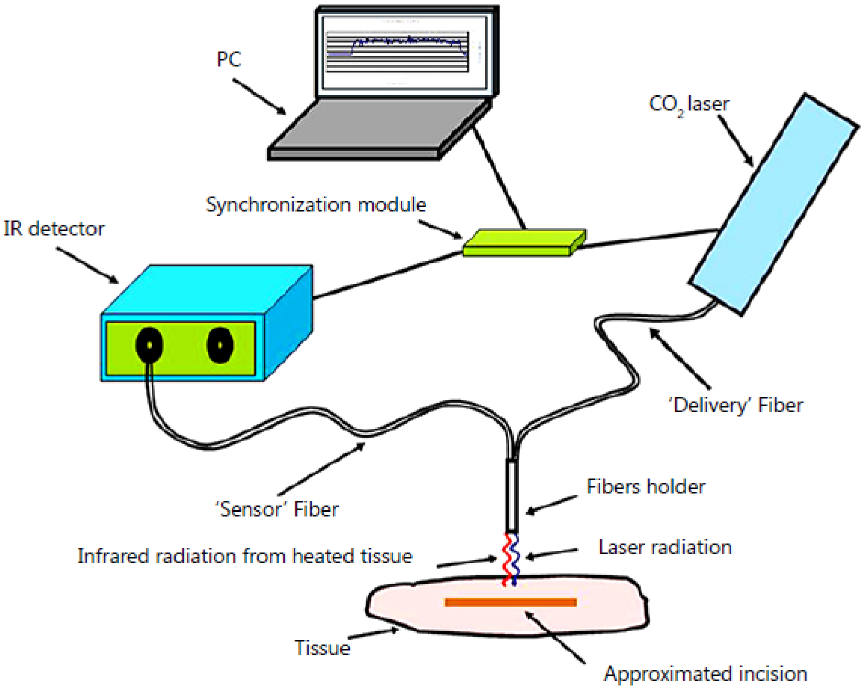


Fig. 28 - Experimental setup for radiometric controlled CO_2 laser corneal welding [101].

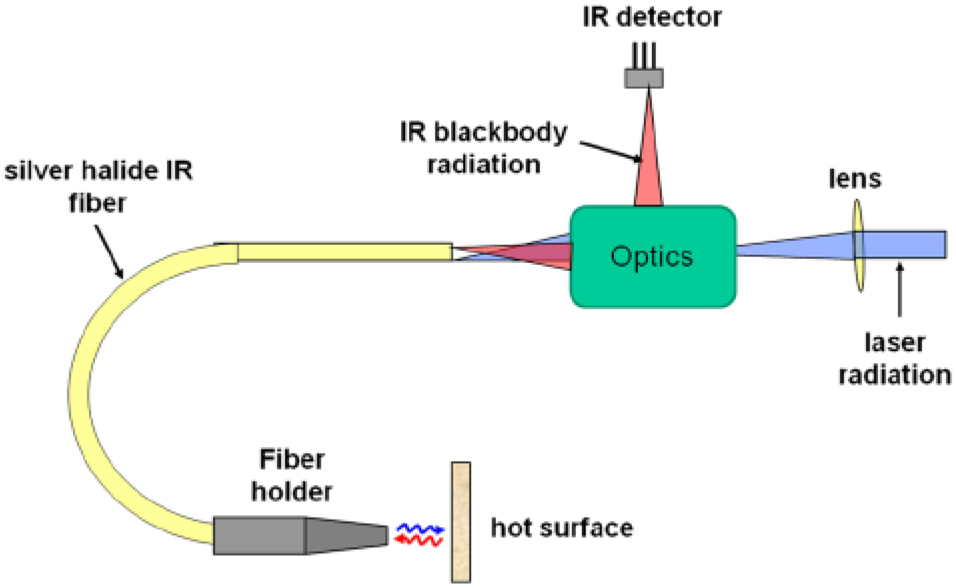


Fig. 29 - The single-fibre laser bonding system [114].

Until the implementation of temperature controlled systems, the end point of the laser procedure was identified by eye surgeons through visual observation of tissue modifications such as bleaching, browning or shrinking [118]. This way, the probability of causing irreversible damages in patient's eye was high. On the other hand, the temperature controlled systems enabled the identification of the ideal temperature for laser operation with minimised thermal complications. Tal *et al.* [40] and Canovetti *et al.* [34] reported that from 50ºC to 60ºC, in NIR diode laser welding procedure, and at 65ºC, in a CO_2 laser welding procedure, photocoagulation occurred with optimal thermal and mechanical resistance results, respectively. Guaranteeing the sealing of ocular closures with improved healing and less inflammatory reactions, these temperatures correspond to the aforementioned soft and moderate laser welding types (**Fig. 21**), enabling the preservation of healthy cornea collagen fibrils. Observing ocular morphology, heat is transferred from the top layer of the cornea to its inner stroma through heat conduction [119]. Studying the temperature distribution inside the eye, Rossi *et al.* [113] presented a mathematical model, solved by FEM, where it was concluded that temperature radial distribution occurred at approximately 250 µm from the heated corneal/air interface, as it is illustrated by **Fig. 30**.

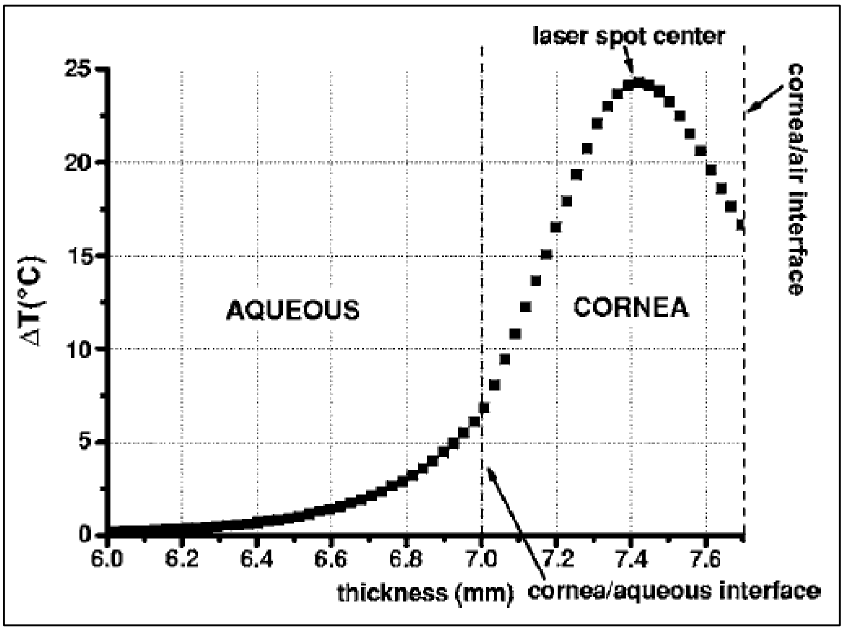


Fig. 30 - Temperature rise distribution along radial distance from the centre of the eye toward cornea/air interface [113].

In addition to the temperature-controlled systems, it is important to consider the optical imaging techniques that retrieve information of laser-tissue mechanisms so that ophthalmologists can adapt the parameters to meet optimal results. Pini *et al.* [120] applied the Multispectral Imaging Autofluorescence Microscopy (MIAM) to obtain data on the reorganisation of corneal structure during the healing process. This technique is characterised by the analyses of fluorescence arising from tissue elements (**Fig. 31**), without any chemical manipulation of the biological samples [24]. Histological and transmission electron microscopy (TEM) observations are also viable, although TEM requires extensive preparation protocols, expensive equipment and limitations in the gathering of three-dimensional information [104]. Contrary to these impractical aspects, Matteini *et al.* [104] utilized atomic force microscopy (AFM) analysis and achieved a refined three-dimensional characterisation of the morphological changes in corneal extracellular matrixes.

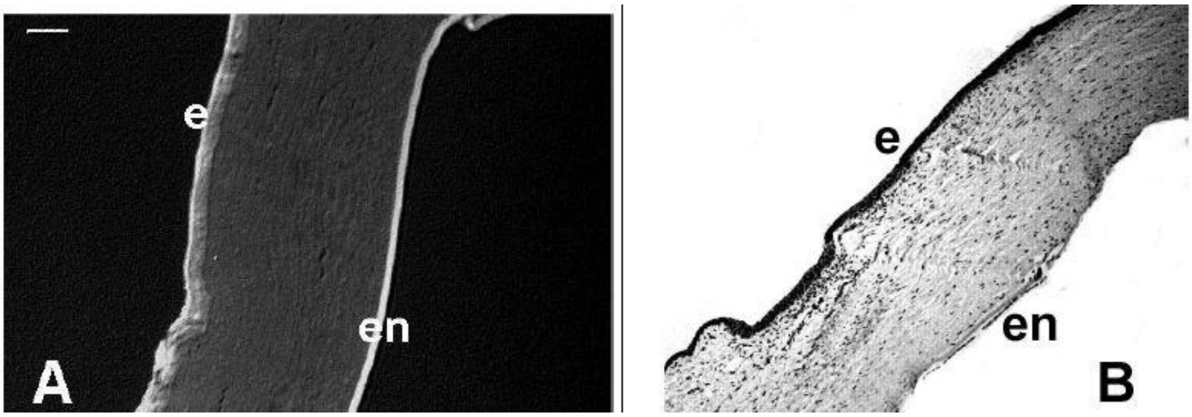


Fig. 31 – Multispectral Imaging Autofluorescence Microscopy of corneal sections. (A) Autofluorescence imaging; (B) Histology imaging; e = epithelium, en = endothelium; bar = 50 μm [120].

5.3.2. Solders, laser-activated dyes and other biologic alternatives

Biological solders and chromophores have an important role in laser welding of ophthalmic tissues as well. Commonly composed of albumin, solders can also be enhanced with chromophores resulting in homogenous or heterogeneous solutions, each one with its own absorption coefficient adapted to the laser type and the defined laser parameters [22,29,42,121]. The purpose of using biologic solutions with chromophores is to better control the laser irradiance, i.e. constraining it in a more precise location of the operating area, since their molecules absorb photons of a particular energy [103,107]. Furthermore, as previously described (**3.1.3 - Solders and laser-activated dyes**), addition of indocyanine green dye to biological solders induce eye closures with lower irradiation fluencies due to an optical dye absorption of approximately between 800 and 810 nm [21]. Both laser soldering and dye-enhanced soldering techniques prevent excessive thermal degeneration of surrounding structures [34,122]. Once more, compatibility between laser and absorber wavelengths is crucial for ocular improved outcomes.

One of the main difficulties in using biological solders in eye surgeries is controlling and obtaining the adequate viscosity of the solution [110]. **Fig. 32** illustrates the complications of applying solders with high viscosity and low viscosity properties, in the optical globe. With low viscosity solders (**Fig. 32a**), the dispersion of the solution outbounds the area of surgical intervention, causing the laser radiation to be absorbed by surrounding healthy tissues [110]. On the other hand, biological solders with high viscosity (**Fig. 32b**) have not the required dispersion within the operating area, and consequently, the laser procedure is not effective, resulting in uneven bonding strengths [35,105].

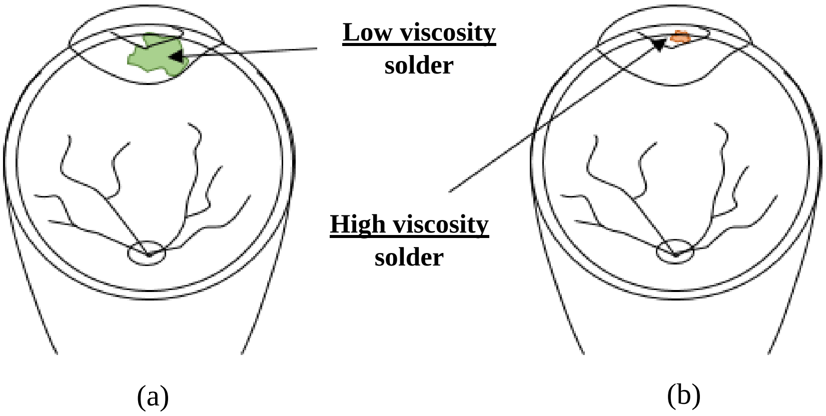


Fig. 32 - Representation of the solders in the eye: (a) Low viscosity; (b) High viscosity.

In order to overcome solder viscosity problems, welding solutions have been presented by introducing new solid/semi-solid formulations [110], nanosolders [22], biologic films [123] and biodegradable adhesives [124].

Chetoni *et al.* [111] produced new solid and semi-solid formulations to ensure the chemical stability of ICG dye, and therefore, to improve the tissue welding procedure. Solid formulations based on tamarind seed polysaccharide (TSP), which were tested in a rabbit model, were found to allow the best performance in terms of corneal tissue repair (improved repair strength and reduced thermal injury). In turn, Rossi *et al.* [22] presented enhanced protein solders with innovative chromophores, such as nanochromophores, creating hybrid structures composed of ICG, specifically, gold nanoshells suspended in albumin fibre. The application of this combination led to excellent chemical stability at high irradiation levels, showing a flexible conjugation of chromophores with standard biological solders.

A different approach was followed by Garcia *et al.* [123] and Pohlenz *et al.* [124], who substituted the use of solid formulations and hybrid protein solutions by biological and biodegradable adhesives. Specifically, Garcia *et al.* [123] sealed lacerations with the utilisation of chitosan films prior to NIR laser closure. These chitosan films are linear polysaccharides derivative from chitin, which, in combination with NIR closure, allow an easier tissue manipulation, lesser time to laceration closure and higher leak pressures. More recently, Pohlenz *et al.* [124] studied the reconstruction of the medial orbital wall with a synthetic, semi-flexible and absorbable composite material denominated Ethisorb. By comparing Ethisorb with the commonly used titanium meshes, Pohlenz *et al.* [124] concluded that this biodegrable patch was more cost-effective and enabled a reduction in the post-operative risk of infection.

As displayed in **Table 13**, which summarises the proposed solutions and the respective results, the spectrum of biologic alternatives is wide and good results have been achieved with laser welding in eye surgery.

Table 13 - – Reported applications and results of the alternative solutions to biological solders.

Study	Surgery	Alternative to solders	Advantages and results
Chetoni *et al.* [110]	Corneal perforations	Solid formulations of TSP containing ICG	Improved repair strength Reduced thermal injury
Rossi *et al.* [22]	Welding of ocular tissues	Gold nanoshells at silica nanospheres suspended in albumin fibre	Excellent chemical stability at high irradiation levels
Garcia *et al.* [123]	Sealing of ocular lacerations	Chitosan films	Easier tissue manipulation Less time to closure Higher leak pressures
Pohlenz *et al.* [124]	Reconstruction of medial orbital	Ethisorb	Biodegradable adhesive No post-operative infection Cost-effective material

5.3.3. Overview of ocular repairs

The strong evolution registered over the last 40 years in ophthalmologic laser welding results from the intense research that has been conducted in this field. A chronological evolution of eye laser welding research is displayed in **Table 14**. The studied laser welding surgeries, their respective parameters and procedures and the obtained results are summarised in the table.

From 1992 to 1994, Williams *et al.* [125] reported the first successful corneal welds in animal and human in vitro models, utilising continuous wave (CW) hydrogen fluoride (HF) laser. However, HF application turned out to be expensive and not widely used in medicine [103,119]. Barak *et al.* [118] used CO_2 laser welding in animal corneoscleral surgery, reporting positive results with no post-operative leakage. The CO_2 laser welding procedure became reliable since no thermal damage was promoted in intraocular tissues. Because the high water content in the cornea and sclera, the laser was found to be mainly absorbed by water molecules [21,119]. By 2001, Pini *et al.* [21] opened the door to the first application of diode laser corneal welding to penetrating keratoplasty, i.e. corneal transplantation. Savage *et al.* [115] achieved continuous wave NIR laser welding of in vitro porcine cornea and sclera tissues utilising an erbium fibre laser with wavelength emissions of 1,455 nm. With this technique, Savage *et al* [115] proved that strong ocular welds can be verified without the application of extrinsic dyes, chromophores or solders, corroborating the recent studies of Lèclere *et al.* [62] and Nakadate *et al.* [56] for nervous and vascular repairs. Three years later, Menabuoni *et al.* [121] studied cataract laser welding surgeries in paediatric patients. By using Seidel tests, the authors concluded that the process was effective, no postoperative leakage was registered, and a reduced healing time was observed.

With the purpose of investigating the potential application of infrared lasers, Rasier *et al.* [116] tested sealing corneal cuts with four types of lasers: 809 nm diode laser with ICG, 980 nm diode laser, 1,070 nm YLF laser and 1,980 nm Tm:YAP laser system. From the experimental study, authors concluded that 1,070 nm and 1,980 nm wavelengths are suitable for beneficial outcomes in corneal welding.

Table 14 also shows that since 2008, the application of eye laser welding technologies expanded to several types of surgeries, such as cataracts, PKP or corneal. These surgeries became more common, since the procedure was verified to be safe, efficient and with overall positive post-operative results in the patient. However, according to Buzzonetti et al. [122], the instrumentation and technical performance of this procedure require specific training since significant differences from conventional surgery exist, mostly because of the learning curve necessary to achieve correct instrument manipulation.

More recently, Heriot [42] conducted an innovative study on retinopexy surgery, by combining thermal fusion with posterior photocoagulation of tissues. As the retina is detached in retinopexy (**Fig. 33a**), the retinal and subretinal space needs to be dehydrated followed by the application of photocoagulation, which consists of using thermal energy to heat the tissues and irradiating cells at a specific wavelength, resulting in immediate reattachment and treatment of the retina without infection associated problems (**Fig. 33b**).

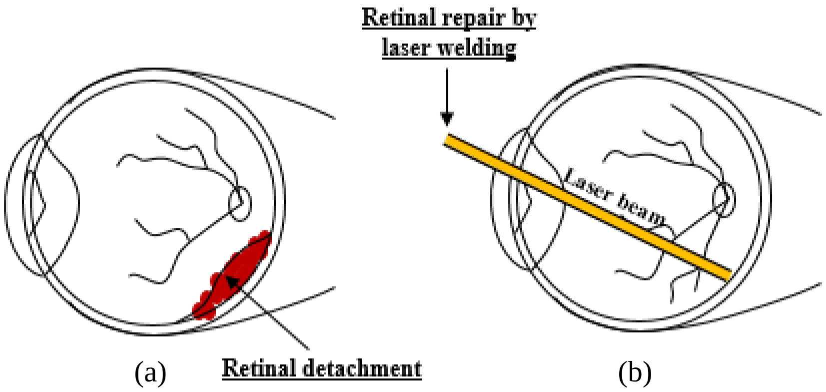


Fig. 33 - Retinopexy: (a) before laser welding surgery; (b) reattachment by laser welding.

Alternatively to Heriot [42] and to the standard laser welding technologies shown in **Table 14**, Umanets et al. [29] had already conducted a research on the retinopexy surgery with the application of high frequency electric welding (HFEW). Although HFEW requires immediate contact between the tip of the handpiece and the treated tissue, this technology allows long-term chrorioretinal connections with the same strength as the conventional laser welding retinopexy and the HFEW instruments are similar to standard laser instrumentation, although no significant advantages over laser procedures were reported.

Table 14 – Chronological evolution of eye laser welding surgeries and respective results.

Study	Surgery	Model	Welding Technology	Solder/Dye	Power (mW)	Results
Williams *et al.* [125]	Cornea	Human	Hydrogen fluoride laser	NR	65-87	Good bonding strength sustaining high intraocular pressure values.
Barak *et al.* [118]	Corneoscleral	Animal	CO_2 laser welding	NR	600	No leakage
Pini *et al.* [21]	Cornea transplant	Human	Diode laser welding (805nm)	ICG	60-90	No thermal tissue damage No post-operative inflammation
Savage *et al.* [115]	Corneoscleral	Animal	NIR w/erbium fibre laser	NR	130-250	Increased tensile strength
Menabuoni *et al.* [121]	Cataract	Human	NIR diode laser (810nm)	ICG	70	No thermal tissue damage No post-operative inflammation
Rossi *et al.* [22]	Cornea transplant	Human	NIR with PLW	ICG	50	Immediate sealing of welding site
Rasier *et al.* [116]	Cornea	Animal	Diode laser welding (809nm) Diode laser welding (980nm) YLF laser (1070nm) Tm:YAP laser (1980nm)	ICG -- -- --	200 1-3 (W) 1-1.5 (W) 38-46	YLF laser (1,070nm) and Tm:YAP laser (1,980nm) showed best results (absence of carbonisation).
Buzzonetti *et al.* [122]	PKP + Cataract	Human	NIR diode laser (810nm)	ICG	NR	No leakage No thermal tissue damage
Canovetti *et al.* [34]	PKP	Human	NIR diode laser (810nm)	ICG	60	Immediate sealing of welding site No post-operative inflammation
Tal *et al.* [40]	Cornea	Animal	CO_2 laser welding	Albumin	NR	No leakage
Heriot [42]	Retinopexy	Animal	Thermofusion with Photocoagulation	NR	NR	Immediate adhesion of chorioretinal connections No leakage

PLW – Pulsed Laser Welding.
NR - Non-referred.

5.4. Main remarks

- Ophthalmic welding technologies have contributed to more effective and efficient, safer, and cost reduced surgeries with the benefits of improving healing processes.
- Thermal feedback systems, welding parameters and type of solder used are the main factors to be considered when using laser welding in ophthalmology surgeries. The importance of the wavelengths compatibility on both laser and absorbed tissue must be a primary concern since it affects the success of the weld.
- A constant evolution has been registered in this field mostly because of the diversity of welding technologies combinations with standard practices.
- The evolution of the laser welding procedures may be focused on the application of nanosolders with specific characteristics to improve tissue laser response in terms of temperature achieved versus the efficiency of the welding.
- Further studies focused on comparing different technologies and testing more diversified models, animal or human, are required so that the already established laser welding procedures, such as NIR diode laser or CO_2 laser welding, are improved, and consequently, the eye surgery impact in the patient's life can be effectively diminished.

6. UROLOGY

As a medical science for healing urinary tract diseases, urology is inevitably associated with organs such as kidneys, urinary bladder, urethra, penis, vagina, prostate or scrotum [46,126]. Wounds or injuries in theses organs can lead to severe infections, constant bleeding and continuous urine leakage thus, surgical interventions are necessary to repair and recover proper biologic function of patient's urologic system.

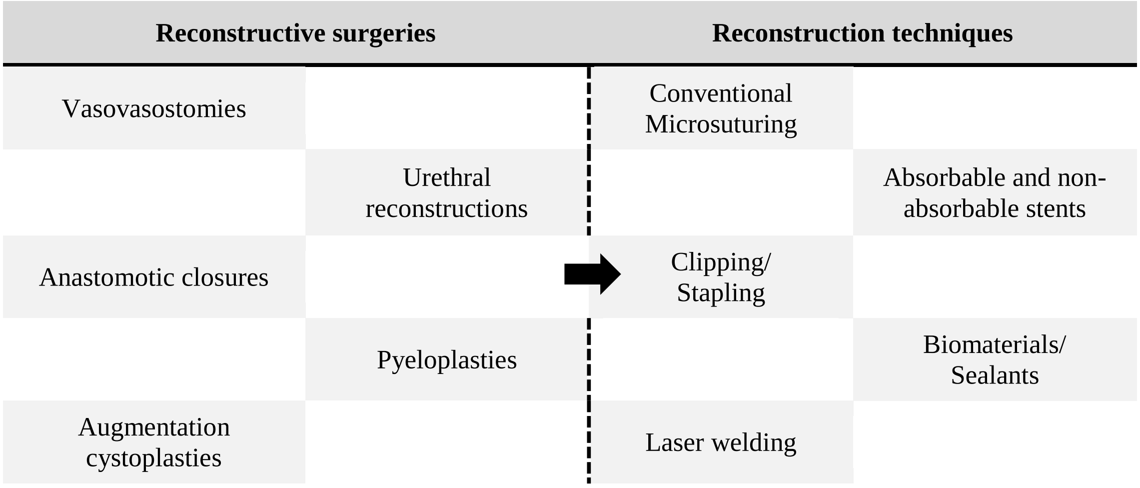
Urology surgeries can either be ablative or reconstructive [45,127]. Ablative procedures such as stone destruction, stricture diseases, prostatic ablation or tumour resection were greatly improved with the laser technology and, to date, there are still reports in the innovation and investigation of the matter [128–130]. However, many problems associated with the urinary tract can also be solved with reconstructive surgery. Implications with clinical urologic reconstruction in some urinary tract organs are still an obstacle to surpass. **Table 15** exposes the most common clinical problems in the main organs that compose the urologic system and their associated suitability for regenerative surgery [131]. This way, the present chapter focus in this type of urologic surgeries and respective literature that allowed the evolution of this medical field in terms of procedures and technologies.

Table 15 – Urinary tract clinical problems and suitability for regenerative surgery (adapted from [131]).

Urinary Tract	Clinical problem	Regenerative surgery
Urinary Bladder	Bladder cancer	Yes
	Neuropathic bladder	
	Intractable idiopathic bladder dysfunction	
	Bladder Exstrophy	
Kidney	Prevalence of chronic kidney disease (CKD)	Yes, but most advances are towards ex vivo applications and are still a long way from a regenerative medicine approach
	Renal trauma	
Penis	Penile reconstruction	Yes, but very limited application, mainly confined to major penile reconstruction. Very unlikely to find a role in ED.
	Erectile dysfunction (ED)	
Urethral Sphincter	Stress or sphincteric weakness urinary incontinence	Yes
Urethra	Hypospadias	Yes, but largely confined to complex or “re-do” cases with limited availability or native tissue.
	Urethral trauma and urethral strictures	

6.1. Reconstruction surgeries and techniques

Urology reconstructive surgeries are mainly based in tissue approximation, nerve coaptations or vascular anastomoses procedures. Vasovasostomies, urethral reconstructions, anastomotic closures (bladder or bowel), pyeloplasties or augmentation cystoplasties are examples of the multitude of common reconstructive procedures [126,127,132,133]. Throughout the years of research in this matter, techniques and instrumentation for such procedures had a strong evolution. According to literature, reconstruction techniques are divided in accordance to **Fig. 34**.



Reconstructive surgeries		Reconstruction techniques	
Vasovasostomies		Conventional Microsuturing	
	Urethral reconstructions		Absorbable and non-absorbable stents
Anastomotic closures		Clipping/ Stapling	
	Pyeloplasties		Biomaterials/ Sealants
Augmentation cystoplasties		Laser welding	

Fig. 34 - Possible reconstructive surgeries and techniques in urology.

Conventional microsuturing, clipping or stapling, utilisation of absorbable and non-absorbable stents, biomaterials and sealants are available reconstruction techniques for urologic procedures. With the laser integration three reconstruction techniques were developed for urologic treatment: (1) laser tissue welding; (2) laser tissue soldering (LTS) and (3) Photochemical bonding tissue. Fried and Matlaga [127] present an excellent summary of their characteristics (**Table 16**).

Despite the medical non-consensus on the most suitable reconstruction technique and device [46,127,131], it is important to understand the evolution and current state of standard urologic surgical instrumentation and robotics.

Table 16 - Comparison of laser tissue welding techniques [127].

	Photothermal		Photochemical
	Laser soldering	**Laser welding**	
Objective	Thermal band-aid	Full-thickness weld	Heat-free weld
Interface	Solder-tissue	Tissue-tissue	Tissue-dye-tissue
Wavelength	808 nm	450 – 1,300 nm	470 nm
Mode	CW	CW or pulsed	CW
Irradiance	High power	High power	Low power
Irradiation time	Short (15s–10 min.)	Short (15s–10 min.)	Long (> 10 min.)
Dye	ICG	With or without dye	Naphthalimides/Riboflavin
Adhesive	Albumin or fibrinogen	None	None
Advantages	Fluid-tight closures	Strong welds	No thermal damage
Disadvantages	Variable solder-tissue adhesion	Thermal damage Inconsistent welds	Variable tissue apposition Longer irradiation times

6.2. Reconstruction instrumentation and robotics

In early years, urologic surgeries were performed as “open surgeries” and complications due to the internal tissues exposure, such as bleeding or possible infections, were most likely to occur. With technological evolution and innovation, the minimal invasive surgeries (MIS) appeared and allowed the diagnosis and treatment of urologic diseases with reduced body surgical exposures. Surgeries as laparoscopy, endosurgery or cystoscopy turned urologic treatment more efficacious with reduced morbidity and convalescence rates [134] despite its drawbacks, such as the time-consuming and the ultimate factor of this innovation: cost.

The mentioned reconstructive techniques in **Fig. 34**, beneficiated from this type of surgery, as it will be verified in the next pages. In the beginning of the XXI century, robotics gave the first steps in various medical fields with the aim to increase the possibilities of such devices. They were integrated in urologic MIS providing advantageous factors such as enhancement of laparoscopic precision, decrease in urologists learning curve and improved dexterity with adaptable motion scaling [126,135,136]. In respect to the laser welding technique, MIS with robotic integration allowed the development of the fibre optical laser delivery technology in laparoscopic surgeries. This new device for minimal invasive procedures, denominated laparoscope or laserscope (**Fig. 35**), allowed a mobility of 360º rotations with flexibility up to a 45º angle [137,138].

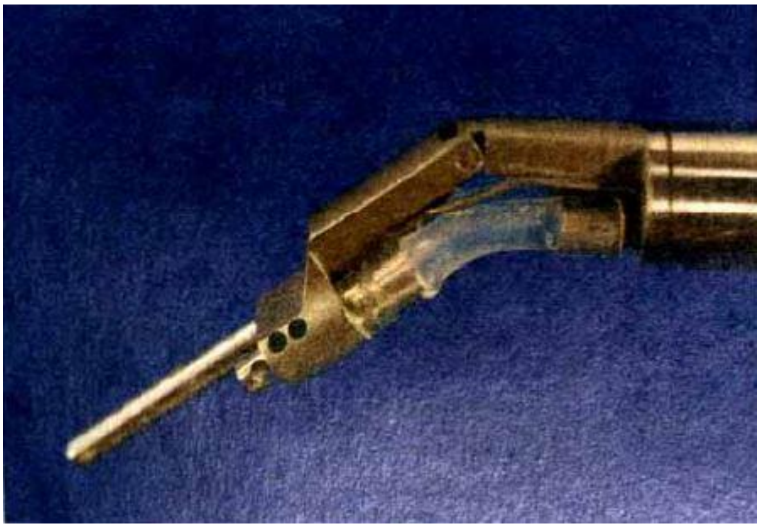


Fig. 35 - Prototype laparoscopic laser delivery device [138].

Accordingly to Gettman *et al.* [135], by 2003, robotic devices in urology included prototypes of endoscopic manipulators, master-slave robotic systems and clinical available robots as well. With recent technology developments, Navaratnam *et al.* [139] study exposes an excellent summary for present robotic devices in the urology field (**Table 17**). When observing **Table 17** it is important to notice that these types of technology allowed the urologist to have more mobility and manipulation over tissues due to the integrated degrees of freedom (DOF), improved grip and image-processing visualisation during such procedures [135,139]. The evolution of image-processing features in endourology and laparoscopic surgery were early reported by Igarashi *et al.* [140] where panoramic and three-dimensional images improved the urologist field of view, depth cue and prevent discontinuous visual information (**Fig. 36**).

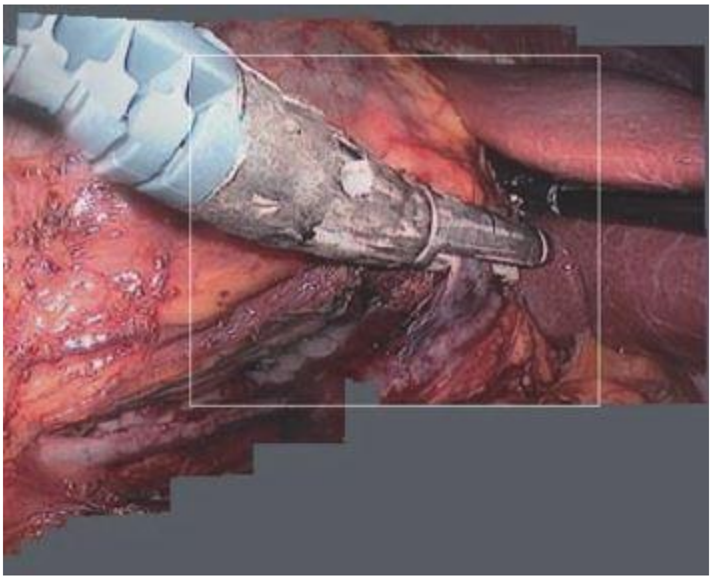


Fig. 36 - Panoramic image processed from laparoscopic video images [140].

Table 17 - Summary of key urological robotic technology [139].

Device name	Designation	Telescope	Robotic arms	Clinical applications
da Vinci™ Xi (Intuitive Surgical Inc., Sunnyvale, CA, USA)	3D binocular viewing console, Endowrist™ finger controls, foot pedals for clutching and application of energy	3DHD 8 mm camera	Four robotic arms hanging from an overhead boom system allowing multiquadrant access	Pelvic surgery, retroperitoneal surgery, intracorporeal reconstruction
da Vinci™ (Intuitive Surgical Inc.) SP 1098	As above Additional foot pedal to allow movement of robotic arms in unison	3DHD 12 mm articulating camera	Boom-mounted single robotic arm with single 25 mm robotic port 6 mm articulating robotic instruments allowing triangulation	Single-port surgery. Cadaveric studies for prostatectomy, cystectomy, and partial nephrectomy complete. US Food and Drug Administration-approved
Revo-i™ (Meere Company, Yongin, Republic of Korea)	3D binocular viewing console, wristed instrument control with hand clutch Foot pedal camera clutch	3DHD 10 mm camera	Four robotic arms mounted to boom Instruments are 7.4 mm in diameter	Only clinical study has been with Retzius-sparing radical prostatectomy
Roboflex Avicenna™ (Elmed Medical Systems, Ankara, Turkey)	Adjustable seat with armrests for surgeon. Joystick controls. Touchscreen to modify speed of deflection, adaption to mode of ureterorenoscope, advancement and retraction of laser fiber, adjustment of irrigation flow rate. Two foot pedals control laser and fluoroscopy	Off-the-shelf existing digital ureteroscope	Robotic manipulator which holds ureteroscope Endoscope stabilized by two holders	Flexible ureteroscopy
Auris robotic endoscopy system (ARES™) (Auris Surgical Robotics, Redwood City, CA, USA)	Video game-like hand controller with electromagnetic-generated real-time navigation	Remote driving fully incorporated flexible digital endoscope	Three robotic arms including camera with multiple channels allowing the passage and control of laser fiber and irrigation	Flexible ureteroscopy
AquaBeam System™ (Procept BioRobotics, Redwood Shores, CA, USA)	Stand-alone with keyboard and touchscreen An input for transrectal ultrasound which maps and plans subsequent prostate resection	22F Rigid Hopkins Cystoscope	Articulating robotic arm that delivers high-pressure saline in longitudinal and rotational movements	Benign prostate hyperplasia

3D, three-dimensional; 3DHD, three-dimensional high-definition.

These technologic innovative devices were revolutionary in many medical fields, and brought enhanced factors such as precision, control and real-time monitoring for more efficient and safe reconstructive interventions. Whether by conventional microsuturing, biomaterials application, sealants application, stents or laser welding, these techniques developed urology with a remarkable impact [127,139,140].

6.3. Conventional microsuturing, clipping, stapling and stents

Despite their disadvantages such as possible foreign body reaction, creation of microscopic urine leakage and tissue ischemia caused by suture knots [45,141,142], substitution of sutures through the application of clips/staples closures and the development of improved suturing devices, as the Endo-Stitch, were beneficial in terms of operative-time, leakage rates and histology, as confirmed by Leppäniemi *et al.* [142] and Wolf *et al* [138] (**Table 18**). On the other hand, laparoscopic suturing and stapling proved to be inaccurate and time consuming, with the latter being inadequate for specific tissue geometries or thicknesses, even though they are of easy application [137,143].

Table 18 - Comparison between suture conventional suture technique with Endo-Stitch and titanium staples.

Study	Surgery	Instrumentation	Remarks
Wolf *et al.* [138]	Ureterotomy closure	Endo-Stitch	Operative-time was 24 min. compared with the 40 min. of suturing. Reduced leakage rates and better histology.
Leppäniemi *et al.* [142]	Ureterotomy closure	Titanium staples	Operative-time was 7 times lower than suturing with similar healing results.

The combination of conventional suturing with non-absorbable and absorbable stents was also tested in animal vasovasostomies procedures with statistically insignificant patency rate results when compared to sutured-only procedures [144,145]. Nonetheless, the role of sutures in urologic reconstructive techniques is still of crucial importance [141,146–149]. Although the inclusion of biomaterials, sealants and laser welding provide better outcomes, sutures are still commonly used for the alignment and stability of tissues prior to LW application with such external auxiliaries.

6.4. Biomaterials and sealants

The application of biomaterials and sealants in reconstructive urologic surgeries mainly focuses on promoting tissue haemostasis, adhesion and urinary tract sealing. Urologic advantages of these techniques include optimal wound healing, supraphysiologic properties, accelerated vascularisation, minimal inflammation with rapid clot formation [136,150–152]. **Fig. 37** illustrates the application of fibrin glue in a partial nephrectomy to seal the patient's kidney.

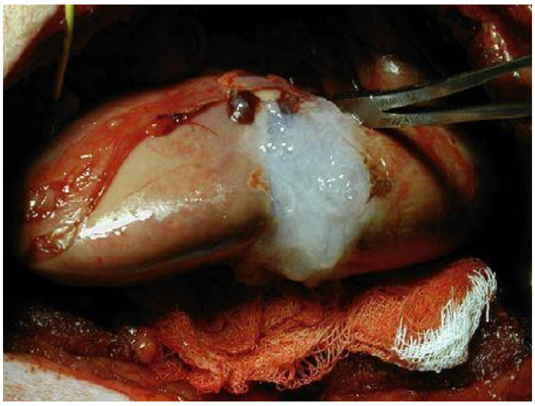


Fig. 37 - Fibrin glue applied to a partial nephrectomy defect in a porcine model [151].

According to literature [136,151,152], fibrin sealants stimulate the coagulation cascade (**Fig. 38**) in order to reach a stable tissue clot with proper characteristics that can withstand biological demands of the respective organ. This suitable and viable clot only results with the addition of an enzyme denominated Factor XIII which allows fibrin cross-linking. Other haemostatic agents are also included in **Fig. 38** coagulation cascade process such as thrombin. The haemostatic agents and tissue adhesives commonly present in reconstructive urologic surgeries are well characterised by Evans and Morey [150], and **Fig. 39** allows the identification of each one of them. Additionally, in **Fig. 39**, it is also possible to notice the presence of some tissue adhesives, already approached for nervous and vascular repairs (**3.1.3 - Solders and laser-activated dyes**), such as cyanoacrylate and polyethylene glycol (PEG).

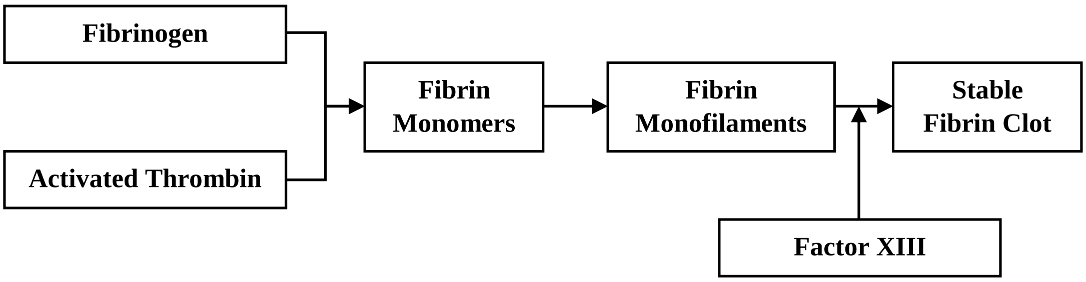
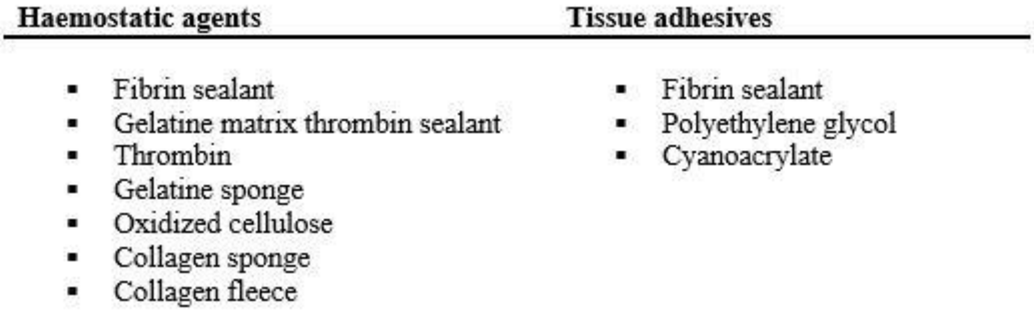


Fig. 38 - Final stages of the coagulation cascade (built based on data from [150, 151]).



Haemostatic agents	Tissue adhesives
▪ Fibrin sealant	▪ Fibrin sealant
▪ Gelatine matrix thrombin sealant	▪ Polyethylene glycol
▪ Thrombin	▪ Cyanoacrylate
▪ Gelatine sponge	
▪ Oxidized cellulose	
▪ Collagen sponge	
▪ Collagen fleece	

Fig. 39 - Haemostatic agents and tissue adhesives for urological reconstruction surgeries [150].

6.5. Laser welding technique in urologic repairs

As seen in previous chapters, since the laser breakthrough in the late 1960s, welding technologies have emerged in various medical fields and urology was also one of them in which laser welding presented to be an innovative and revolutionary technique, specifically in the urinary tract ablative and reconstructive surgeries. By 1966, ophthalmology and dermatology had already reported successful results in the welding of detached retinas and skin cancer treatments [45,153].

The introduction of laser welding as an alternative technique for tissue reconstructive procedures allowed the achievement of immediate watertight seals, avoidance of lithogeny related problems, reduced operative-times and inflammations [133,143,154,155]. However, as seen in other medical fields, this integration requires two important factors: financial investment in such technologies and medical experience for better and successful procedures [132,156,157].

Focusing in the types of lasers mostly utilised in this technique, for urologic treatment, many studies of CO_2, argon, Nd:YAG, Ho:YAG, diode lasers and potassium-titanyl-phosphate (KTP) lasers have been widely recognised for their successful experimental and clinical procedures [146,156,158].

In this matter, early studies by Jarow *et al.* [159] and Peron and Farah [160] were performed with CO_2 and Nd:YAG lasers achieving good healing results, such as patency and fertility, for animal models. The pioneer urologic work with CO_2 laser tissue welding was achieved by Poppas *et al.* [161] and Ganesan *et al.* [162]. The authors performed urethral reconstructions with the addition of protein solders reducing operative-time by 30% with improved weld tensile strengths and success rates of 90% [161] and 65% [162] against the 50% success rates with conventional microsuture methods.

Parallel to these studies, comparison between CO_2 and Nd:YAG laser tissue welding application was made by Shanberg *et al.*, concluding that Nd:YAG laser was unsuitable due to the same factors mentioned in **3.1.2 - Overview of nervous and vascular repairs**: deep transmural necroses, carbonisation of tissue and instable tissue fusions [51,54,63]. The curiosity and feasibility of the CO_2 laser for the reconstruction of urethral tissue led to the investigation of optimal welding parameters, by Poppas *et al.* [163]. In their study, weld highest burst strengths and low stricture complications were achieved when power and laser pulse duration settings were of 120 mW and 100 msec, respectively.

The utilisation of other developed lasers such as diode lasers or KTP lasers was later introduced in the urologic field when laser-tissue bonding interactions and associated thermal damage started to be investigated.

6.5.1. Bonding interactions and thermal damage

Despite the successful LTW experimental and clinical results, the understanding of this tissue approximation technique, in urology, was not clear, specifically the bonding interactions that were involved in the tissue weld [133,164,165]. Factors such as weld end point were only visually perceptive to urologists as light tan, blanching or whitening of welded tissues [138,143,163,165,166]. Thus, corroborating the Menosky *et al.* [55] and Chuck *et al.* [68] visual identification scores previously referred for nerve and vascular repairs (**3.1 - Laser welding technique**).

Therefore the introduction of chromophore laser-absorbing dyes in this technique permitted to diminish this problem in two dimensional laparoscopic laser welding surgeries since three dimensional visualisation devices require higher financial investments [137,143,148]. These dyes have improved urologic LW applications and differentiated LTW from a newly approach denominated LTS in which a chromophore laser-absorbing dye is incorporated in a solder protein solution (**Table 16**). This way, the LTS technique permitted the control of laser energy distribution and consequently minimised tissue thermal damage since fluorescence characteristics were only present in stained tissues (**Fig. 40**).

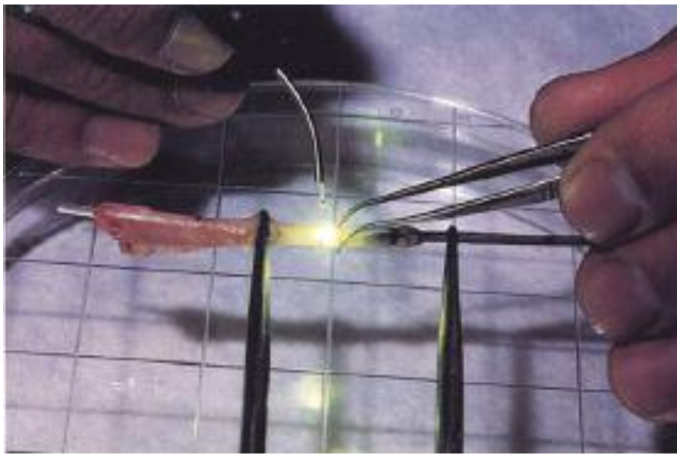


Fig. 40 - Application of KTP-532 laser welding with ICG (fluorescence effect) [143].

Additionally, higher bursting pressures and tensile strengths were also verified with the application of this technique [137,146,154]. The consolidating welding guidelines from the extensive studies in this matter, allowed to decrease laser setting powers through directly chromophore-dyed stained tissues before solder application due to the increased tissue laser absorption results [137,141,143].

Following the interest in the laser tissue welding technology, an important study by Kirsch *et al.* [147] achieved the first successful human urinary tract reconstruction. Reduced operative-time and leak pressures 4.5 times higher than conventional microsutures were excellent encouraging results for the practice of this technique. Laser tissue soldering was also applied in the first successful study for vasectomy reversal procedures, with 90% and 82% patency rates for vasovasostomy and epididymovasostomy, respectively [132].

In terms of associated tissue thermal damages, not only the chromophore laser-absorbing dyes were effective to estimate a suitable weld end point but thermal control devices were certainly an improvement in this matter [45]. LOBIK *et al.* [164] utilized the CO_2 thermal controlled laser welding system for bladder reconstruction surgery with 94% successful healing rates. This system controlled the welding temperature around the 70ºC which resulted in suitable welds and it was similar to the systems described in ophthalmic repairs (**5.3.1 - Thermal control and image-processing**), having two-silver halide fibres made of polycrystalline silver halides due to their flexible, non-toxic and biocompatible properties. An identical thermal feedback system was developed by Shumalinsky *et al.* [167] to improve laparoscopic CO_2 laser soldering in the repair of ureter junction obstruction of animal models. Controlled temperature of the weld at 65ºC produced results with no urinary leakage, strictures or thermal damage (**Fig. 41**).

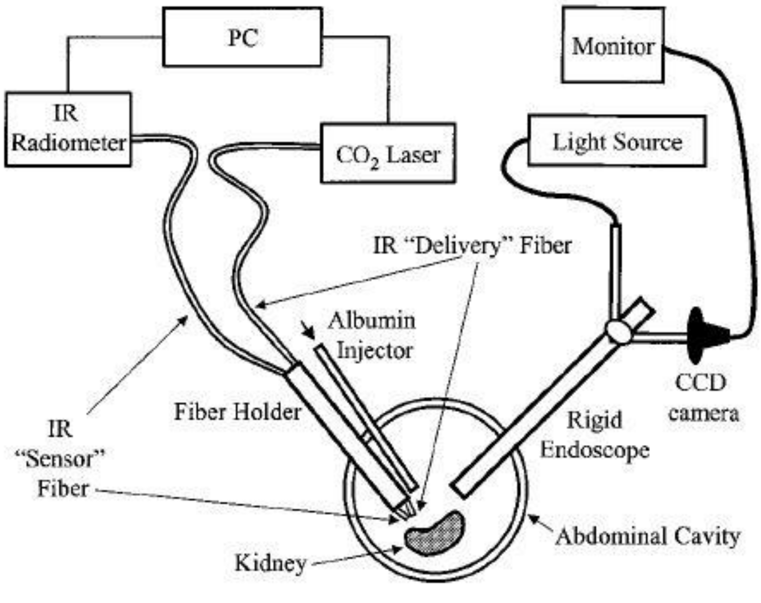


Fig. 41 - Schematic drawing of laparoscopic laser soldering system [167].

Nonetheless, it is also possible to observe that sutures in urologic reconstructive techniques had an important role in the assurance of tissue edge approximation and weld tensile strength.

As previously stated, although laser welding provides better outcomes with protein solder solutions and with chromophore enhanced laser-absorbing dyes, in urology, sutures are still commonly used for the alignment and stability of tissues prior to LW application with such external auxiliaries. With the purpose of evaluating suture mechanical behaviour with laser techniques, Kirsch *et al.* [168] studied the combining effect of diode laser welding with dye-enhanced glue on the tensile strength of placed support sutures and concluded that exposure times longer than thirty seconds decreased the suture tensile strength significantly. In accordance to these findings, in Kirsch *et al.* [148] report, suture disruption also occurred in dyed sutures.

According to literature research, an interesting fact in bladder and urothelial procedures, is that 70% of the tensile strength is achieved in two weeks whereas for skin wound healings, only 30% is reached. Therefore the application of support sutures could be avoided in sutureless urologic procedures [141,148] such as LW with increased tensile strength results. Late 1990s experimental studies [138,164] verified the feasibility of suture-free laser welding technique.

On the other hand, a study by Lee and Gianduzzo [156] concluded that laser welding laparoscopy for pyeloureteral anastomosis was not advantageous over suturing technique. Laser welding of vesicovaginal fistulas was also early reported in 2001 [169] and recently confirmed its feasibility by Dogra and Saini [158] with a more clear interpretation of this LW urologic application. Dogra and Saini [158] carefully analysed the pre-operative and post-operative crucial factors for a successful procedure and could also determine that the LW technique was only effective to small fistulas with less than 4 millimetres.

6.5.2. Overview of laser welding technique in urology

As previously mentioned, reconstructive surgeries are of great importance in urology due to their possibility of recovering a patient’s urinary tract or even undue patient’s past decisions of having children with vasovasostomy or vasoepididymostomy procedures. This way, and according to literature research reports [135,137], surgical applications of the laser tissue welding technique corresponded with surprising and improved results over the conventional reconstructive techniques.

MIS (as the previously mentioned endoscopy, laparoscopy or robotic-assisted procedures) for augmentation cystoplasties, ureteroureterostomies and anastomotic closures or reinforcements, can also be added to the list of surgeries, mentioned so far, with demonstrated success of this technology in the urology field [96,104,128].

Parsons et al. [153] study was one of the firsts to present the effect of the laser in dog bladders, confirming this way the possible and successful integration of laser surgeries in the urologic field. Throughout the 1990s, the urologic laser application stimulated scientific investigations on the types of lasers suitable and feasibility of urethral reconstructions. These extensive studies led to the first report of laser-assisted vasovasostomy in large number of human patients by Shanberg *et al.* [170] with no post-operative complications such as sperm granulomas or inflammations. **Fig. 42** presents a chronologic evolution of breakthrough investigation remarks, between the 1980s and the turn of the century, for the LTW technique in urology.

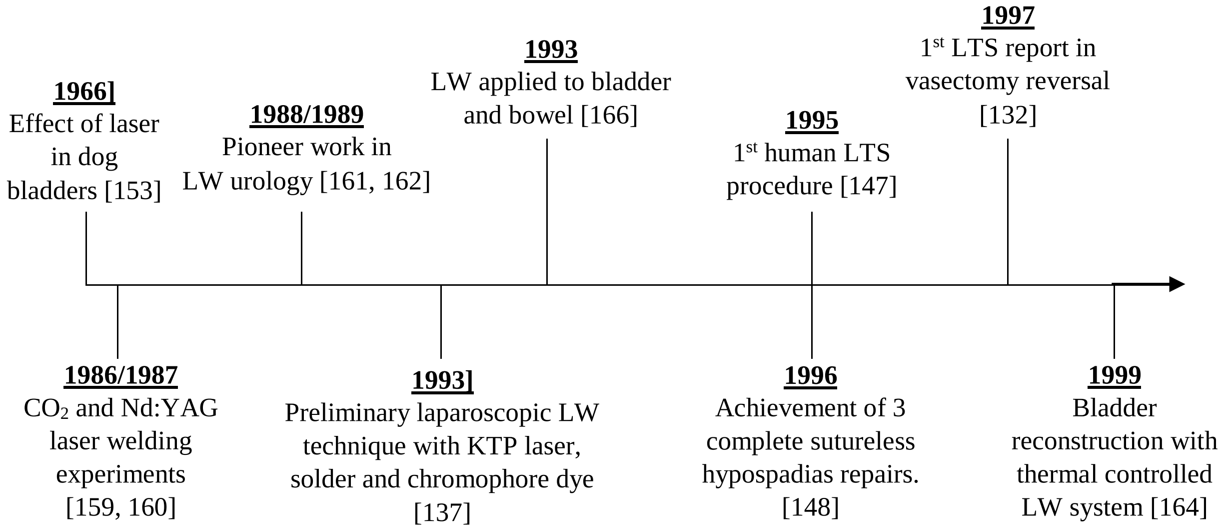


Fig. 42- Main milestones in urology reconstructive surgery, in XX century.

An overview of these results achieved with laser welding in urologic reconstruction is summarised in **Table 19** with the inclusion of the different solder solutions applied and the respective conclusions of the studies exposed so far.

Table 19 - Overview of reconstructive urologic surgeries with laser welding, in the XX century.

Study	Model	Surgery	Technique	Support sutures	Remarks
Jarow *et al.* [159]	Humans (in vitro) and Sprague-Dewley rats (in vivo)	Vasovasostomy	LAVA$_2$	Yes	Equivalent patency and fertility in comparison with conventional suture technique.
Peron and Farah [160]	Sprague-Dewley rats	Vasovasostomy	CO_2 laser	Yes	The technique establishes good mucosal anastomosis.
Vincent *et al.* [171]	Animal (Rat and rabbit)	Vasovasostomy	Nd:YAG laser	N.R.	The technique demonstrated adequate healing process.
Poppas *et al.* [161]	Sprague-Dewley rats	Urethral reconstruction	CO_2 laser CO_2 laser + solder	Yes	CO_2 laser welding success was 58% and with protein solder success was 90%.
Ganesan *et al.* [162]	Sprague-Dewley rats	Patch graft urethroplasty	CO_2 laser + solder	Yes	Success rate of laser welding with protein solder was 65%. Operative-time reduced by 30%.
Bürger *et al.* [172]	Sprague-Dewley rats	Longitudinal urethral incisions	CO_2 laser Nd:YAG laser	Yes	Nd:YAG was unsuitable for tissue welding. CO_2 with similar results as conventional microsuture.
Merguerian *et al.* [154]	New Zealand white rabbits	Hypospadias repair	Diode laser (808nm) + solder + ICG dye	Yes	Increased strength of welded anastomoses. Reduced operative-time, no foreign body reactions.
Poppas *et al.* [163]	Sprague-Dewley rats	Urethral reconstruction	CO_2 laser + solder	Yes	Power settings of 120 mW with 100 msec duration allowed higher bursting strengths with minimised tissue damage.
Poppas *et al.* [137]	Animal (Dogs)	Ureter reconstruction	KTP-532 laser + solder + dye	No	Chromophore application can determine weld end point. It was useful for preliminary stage in laparoscopic tissue welding technique.
Perito *et al.* [166]	Sprague-Dewley rats	Enterocystoplasty	CO_2 laser + solder	Yes	Operative-time reduced by 38%. Laser welding of bladder and bowel achieved.

LAVA$_2$ – Laser-assisted vasovasostomy

Table 19 - Overview of reconstructive urologic surgeries with laser welding, in the XX century (*Cont'd.*).

Study	Model	Surgery	Technique	Support sutures	Remarks
Kirsch *et al.* [146]	Animal (Dogs)	Extravesical reimplantation of ureter	Diode laser (808nm) + solder + ICG dye	Yes	No foreign body reactions with higher burst strength after 7 days. Laser welding is effective in closing vesical muscle flaps over submucosal ureters.
Kirsch *et al.* [147]	Human	Urinary tract reconstruction	Diode laser (808nm) + solder	Yes	First human use of laser tissue soldering in urology. Leak pressures 4.5 times higher. Reduced operative-time.
Kirsch *et al.* [141]	New Zealand white rabbits	Patch graft urethroplasty	Diode laser (808nm) + solder + ICG dye	Yes	Reduced operative-time. Higher leak pressures and weld tensile strength.
Kirsch *et al.* [148]	Human	Hypospadias repair	Diode laser (808nm) + solder + dye	Yes	Three hypospadias repairs were completely sutureless. Laser tissue soldering is feasible, safe and easy to perform.
Kirsch *et al.* [149]	New Zealand white rabbits	Full-tubed skin graft urethroplasty	Diode laser (808nm) + solder	Yes	Reduced operative-time. Leak pressures 7 times higher and excellent tensile strengths. Easy performed and watertight seal welds.
Wolf *et al.* [138]	Animal (Pigs)	Laparoscopic closure of ureterotomy	Endo-stitch Fibrin glue KTP laser + solder + dye	No	Fibrin glue was the most suitable method despite the reduced operative-time of laser welding (7-13 minutes).
Seaman *et al.* [132]	Sprague-Dewley rats	Vasovasostomy and epididymovasostomy	Diode laser (808nm) + solder	Yes	First report of successful LTS in vasovasostomy and epididymovasostomy, with 90% and 82% patency rates, respectively.
(LOBIK *et al.* [164]	Sprague-Dewley rats	Bladder reconstruction	CO_2 laser with controlled temperature system	No	94% successful results were observed with suitable healing of the tissues.

Accordingly to this literature research, the evolution of the laser welding technique as shown to be of slow progression mostly due to four predominant factors: (1) the available low-cost and easy suture, staples or biologic adhesives techniques [133]; (2) the development of enhanced tissue bonding through photochemical procedures [127]; (3) a minor number of studies in urologic LW achieved clinical stages [131]; (4) the development of nanomedicine [173].

The photochemical tissue bonding technique is already known for its advantageous absence of thermal tissue damage. However the development of such technique does not directly implies the resolution of the experimental studies translation into clinical practices.

Many authors report that, to date, despite the large number of urologic laser welding studies the clinical practice still presents low rates in this field [127,131]. Wezel *et al.* [131] perspective, in this matter, is that biological tissue bonding promoted through cellular thermal or chemical modifications has yet to surpass mentioned standard techniques in long-term clinical studies.

To accomplish such achievement, the development of the nanomedicine in the urology field was a major contribution with main applications in urologic imaging-processing, thermal ablation, gene therapy, drug delivery or enhancement of laser-activated solders [46,155,173,174]. An example of the advantageous role of nanotechnology is Huang *et al.* [155] recent report where laser welding technique was applied with a plasmonic polypeptide nanocomposite solder. This innovative approach demonstrated to produce welds with higher photochemical stability, minimum diffusivity and higher NIR absorption by the welded cross-section which translates in a more efficient conversion of light into heat, surpassing this way, one of the most common dyes applied with LTW, the indocyanine green.

Not only these four factors resulted in the slow progress of laser welding technique as a common reference for clinical urology practices but recent development in breakthrough technologies such as three-dimensional printing, combined surgical handpiece devices and augmented reality, played their part into a new biotechnological path for the urology field.

6.6. Future directions

Recent reports in technological innovations for biological integration mark new approaches in urologic reconstruction techniques and instrumentation devices. The three-dimensional printing technology applied to the urologic field, as reported by Parikh and Sharma [175] review, exposes an overview of the most common kidney and prostate related applications. Additionally, three-dimensional printing bio-integration embraces and explores the urologist medical education, facilitates pre-operative planning and enables artificial organs implementation [175].

In other perspective of the urology technological innovations, augmented reality robot-assisted surgeries solidify the already mentioned image-processing revolution from the beginning of the century. Porpiglia *et al.* [176] study applied a real-time monitoring technique with the hyper-accuracy three-dimensional reconstruction (HA3D^{TM}) technology, achieving an enhancement of overall procedure results (**Fig. 43**).

Fig. 43 - Intraprostatic surgery with HA3D^{TM} [176].

Apart from the three-dimensional printing and the augmented reality practices, new instrumentation devices are also being developed and tested. Recent reports [177,178] presents the first device to combine ultrasonically generated heat energy and advanced bipolar energy, the ThunderBeat (TB). This new addition to handpiece devices that can perform sealing and cutting of soft tissues allow better results for welding and dissection procedures with precise control and good haemostatic results. In 2004 [179] and 2007 [180], a similar handpiece device had already been studied in urology for the division of left renal vein branches and intestinal anastomosis with bipolar electrode welding systems denominated ligasure systems, a device utilised in the previously studied tonsillectomy welding procedures.

6.7. Main remarks

- Urology ablative and reconstructive surgeries have been in constant improvement since the laser breakthrough in the 1960s. Laser ablative procedures such as stone destruction, stricture diseases, prostatic ablation or tumour resection were greatly improved. On the other hand, reconstructive procedures also beneficiated from this innovation with the laser welding technique.
- Reconstruction instrumentation evolved due to the development of minimal invasive surgeries and image-processing that were later enhanced with integration of robotics in the medical field.
- Reconstructive techniques such as conventional microsuturing, stapling/clipping, non-absorbable and absorbable stents, inclusion of biomaterials and sealants or laser welding techniques are available for urologic treatments.
- The laser welding role in the urology field as had a slow progress despite the numerous experimental studies with successful results. This delay for laser welding clinical practice is due to mainly four factors: (1) the available low-cost and easy suture, staples or biologic adhesives techniques; (2) the development of enhanced tissue bonding through photochemical procedures; (3) a minor number of studies in urologic LW achieved clinical stages; (4) the development of nanomedicine.
- Future directions of urologic disease treatment may potentially include three-dimensional printing, augmented reality and new instrumentation devices that combine ultrasonically generated heat energy and advanced bipolar energy, such as the ThunderBeat.

7. DENTISTRY

Oral and maxillofacial surgery have been in constant evolution throughout the years. Whether it has been in performing simple tooth extractions to complex procedures as implant surgeries, the control of optimal parameters in the pre-operative, intra-operative and post-operative stages led inevitably to more sustainable and efficient procedures practiced, to date [181]. The revolution and integration of welding techniques in medical dentistry allowed and guided some of the technological advances exposed in the present chapter.

Since 1963, research development for the application of lasers in the dentistry field has brought significant advancements in oral and maxillofacial surgery. The multiple applications of lasers in dentistry make them a resourceful technique for oral intervention. Soft tissue and hard tissue surgeries, biostimulation with low-level laser therapies, as well as welding of orthodontic materials, dental bridges or the curing of implant composite materials, are other innovative and improved applications that were developed with the integration of laser technology [182–184].

According to literature research, in the XX century, the utilisation of lasers was centred in CO_2 and Nd:YAG. Willenborg [182] continuous research, since its integration in 1968, allowed the first CO_2 surgical use in dental literature by 1977. Additionally, Coleton [185] states that the first Nd:YAG laser fibre optic delivery in periodontal surgery was achieved by 1985, two years after Nd:YAG integration in oral surgery. Nonetheless, Coleton [185] also mentions that in the late 1990s erbium lasers began to be applied in cavity preparation and caries removal. A chronological evolution overview of lasers integration in the XX century is illustrated by **Fig. 44** [182–185].

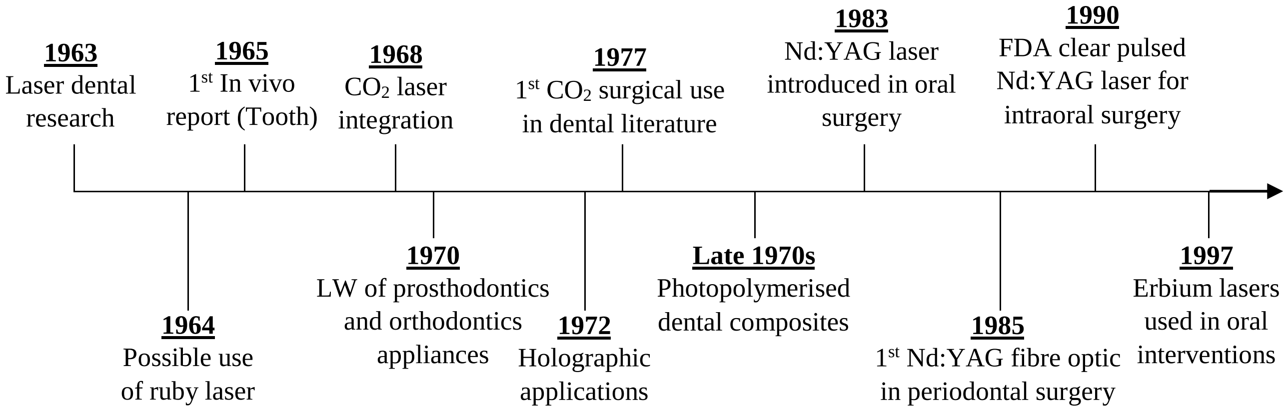


Fig. 44 - Chronologic milestones of lasers integration in the XX century urology field (built based on data from [182-185]).

7.1. Oral tissues, lasers and laser welding technique

Despite this innovative breakthrough in the dentistry field, by 1995 lasers were mainly applied in soft tissue surgery and dental composite curing since the multitude of the already mentioned applications had not been clinically realised [183].

The evolution of laser applications was only possible to be achieved with the study of irradiation parameters such as wavelength, pulsed energy, spatial and temporal characteristics and optical properties of oral soft tissues and dental hard tissues [184]. In early years, the main limitation was centred in the inadequate interaction of lasers with calcified tissues such as dental enamel, cementum and dentin. Therefore, the analysis of optical properties such as refractive indexes, scattering or absorption coefficients were of significant importance [186], as illustrated by **Fig. 45**.

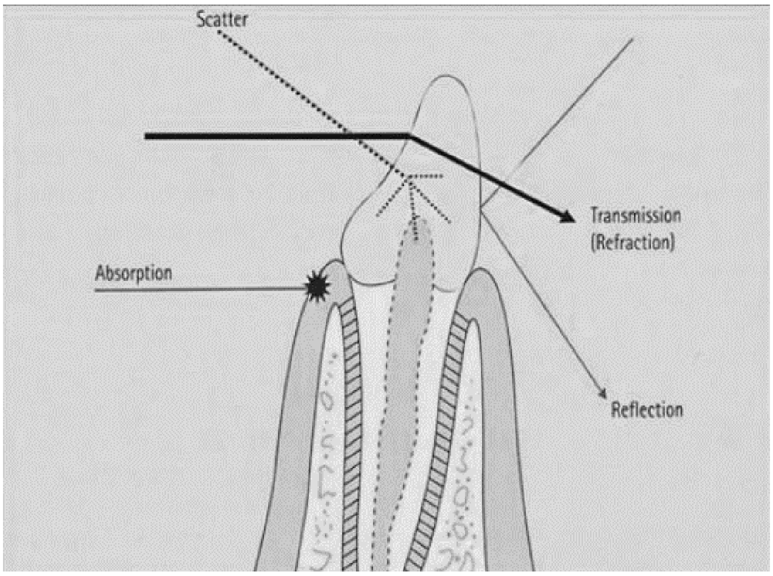


Fig. 45 - Laser light target tissue interactions [186].

From literature research it is possible to observe that, with the transition to the XXI century, dentistry surgery started to be differentiated in two distinct categories: soft tissue procedures and dental hard tissue procedures [185].

Addressing soft tissue, the most common surgeries are gingivectomy, gingivoplasty, frenectomy, free gingival graft, laser peel and soft tissue crown lengthening. Medical interventions with CO_2, Nd:YAG, diode or argon lasers demonstrated to be advantageous in terms of haemostasis, tissue healing, bacterial reduction, post-operative pain and swelling [185,186]. Nevertheless, one of the concerns in oral soft tissue surgeries is the possible associated damage to adjacent bone and teeth structures, and so protection of these hard tissues is also needed [183,187].

With the objective of confirming the suitability of lasers in oral soft tissue welding techniques, Sato *et al.* [187] performed closure of gingival flaps with CO_2 laser welding achieving a sealing with no leakage or tissue inflammation, also demonstrating improved results over conventional suturing.

In terms of dental hard tissues, most common surgeries focus on tooth structure modifications more precisely in dental enamel, cementum and dentin. Due to the ten year gap studies found within literature research on the laser role in this medical field [183–185], it is possible to observe its evolution and therefore observations of the ultrastructural and crystallographic transformations concluded that these are only performed with increased irradiation intensities due to the absorption wavelengths of these tissues being in the range of 9.0 µm and 11.0 µm. Additionally, the utilisation of pulsed lasers is preferred allowing the action of absorbed laser wavelengths in fusion, healing and recrystallization processes without affecting the dental pulp. According to these studies, lasers such as CO_2, erbium, hydrogen fluoride (HF) and excimers are suitable for dental hard tissue interventions, however with specific wavelengths differentiation between them.

Bhatt *et al.* [184] exposes the wide variety of lasers in dentistry applications with an excellent overview of the main clinical applications, advantages, wavelength ranges and tissue absorption characteristics, as well as the important distinction of emission modes of each laser, as aforementioned (**Table 20**).

Similar to thermal tissue interactions mentioned in previous chapters for soft tissues, in dental hard tissues these interactions have also been verified by Fowler and Kuroda [188] and more recently by Bhat [184], however with different thermal profiles than the ones presented for soft tissue laser welding. In their study, Oho and Morioka [189] identified protein decomposition and denaturation of tooth structures at temperatures ranging from 100ºC to 650ºC. On the other hand, recrystallisation was observed from 650ºC to 1100ºC. Analysis of these temperature related modifications showed interesting observations in tooth permeability:

- **100ºC – 650ºC** → Increased acid resistance by chemical changes while demonstrating higher permeability in tooth structure.
- **>1100ºC** →Decreased permeability of enamel while decomposition produces phases susceptible to acid dissolution.

Table 20 - Laser wavelengths used in dentistry [184].

Laser	**Argon**	**Diode**	**Nd:YAG**	**Ho:YAG**	**CO$_2$**	**Erbium family (ErCr :YSGG, Er:YAG)**
Active medium	Argon gas	Solid semiconductor crystals/wafer composed of aluminium/indium, gallium and arsenic (GaAlAs, InGaAs)	A solid garnet crystal combined with rare earth elements yttrium and aluminium doped with neodymium ions	A solid crystal of YAG (yttrium aluminium garnet) sensitized with chromium (Cr) and doped with holmium and thulium ions	A mixture of CO$_2$, helium (He) and nitrogen (N$_2$) gases in proportions 8:7:1	1. ErCr:YSGG (erbium chromium: yttrium scandium gallium garnet): A solid crystal of YSGG doped with Er Cr 2. Er:YAG (erbium: yttrium aluminium garnet): A solid crystal of YAG doped with Er
Wavelength	There are 2 emission wavelengths used in dentistry (both are visible to the human eye): (i) 488 nm (blue) (ii) 514 nm (blue-green)	Available wavelengths for dental use (placed at the near infrared portion of the invisible non-ionizing spectrum): (i) 655 nm (a visible red diode) (ii) 800-830 nm (AlGaAs) (iii) 980 nm (InGaAs, GaAlAs)	1,064 nm (placed in the invisible near-infrared portion of the electromagnetic spectrum)	2,100 nm (placed in the near-infrared portion of the invisible non-ionizing radiation spectrum)	Three emission wavelengths exist (placed at the end of mid-infrared invisible non-ionizing portion of the spectrum): 9,300 nm; 9,600 nm and 10,600 nm	Two emission wavelengths exist (Both the wavelengths are placed at the beginning of the mid-infrared, invisible and non-ionizing portion of the spectrum): (i) 2780 nm (ErCr:YSGG) (ii) 2,940 nm (Er:YAG)
Delivery system	Fibre-optic cable Non-contact mode Contact mode	Fibre-optic cable used in contact mode (for soft tissue surgery) and non-contact mode (for deeper coagulation)	Fibre-optic cable Contact mode Non-contact mode	Fibre-optic system	Hollow waveguide with a hand-piece in contact/non-contact modes	Fibre-optic cable (for ErCr:YSGG) Hollow waveguide/fibre-optic bundle (for Er:YAG)
Emission mode	Continuous wave and gated pulsed modes	Continuous wave and gated pulsed modes	Free running pulsed mode	Free running pulsed mode	Continuous/gated pulsed mode	Free running pulsed mode

Table 20 - Laser wavelengths used in dentistry (*Cont'd.*) [184].

Laser	Argon	Diode	Nd:YAG	Ho:YAG	CO_2	Erbium family (ErCr :YSGG, Er:YAG)
Tissue absorption	Both wavelengths have poor absorption in dental hard tissues and in water. The 488 nm blue light activates camphorquinone, the most commonly used photoinitiator in light cure composites, and light activated impression pastes and bleaching gels. The 514 nm blue-green light has its peak absorption in haemoglobin, hemosiderin and melanin.	Highly absorbed by pigmented tissue. Relatively poorly absorbed by tooth structure.	Highly absorbed by melanin but is less absorbed by haemoglobin than the argon laser. Approximately 90% transmitted through water.	Absorbed by water 100 times greater than Nd:YAG. Ablates hard calcified tissue at high peak powers. Does not react with haemoglobin or other tissue pigments.	Highest absorption in hydroxyapatite than any other dental laser, about 1,000 times greater than erbium and is well absorbed by water, second only to the erbium family. It has shallow depth of penetration into tissue (100-300 micrometer deep).	Both the wavelengths have the highest absorption in water in comparison with other dental laser wavelengths and have a high affinity for hydroxyapatite (Affinity of Er is 20% higher than Er, Cr).
Clinical applications	Both wavelengths can be used as an aid in caries detection. When the argon laser light illuminates the tooth, the carious area appears as a dark orange-red colour and is easily discernible from the surrounding healthy structures. Polymerization of light activated composite resins, dentin bonding agents, sealants, bleaching gels and light-activated impression materials. The 514 nm green light argon is used to perform soft tissue procedures: gingivoplasty, gingivectomy, crown lengthening and troughing. Treatment of highly vascularized lesions such as haemangiomas, coagulation and haemostasis.	The 655 nm visible red diode is used to analyse and quantify the degree of caries. Soft tissue surgeries like cutting and coagulating gingiva and oral mucosa. Sulcular debridement.	Cutting and coagulating dental soft tissues. Sulcular debridement removal of pigmented surface carious lesions haemostasis. Treatment of aphthous ulcers pulpal analgesia.	Frequently used in oral surgery for arthroscopic surgery on the TMJ. Also, has many medical applications.	Primary dental applications are soft tissue procedures such as: gingivectomy, gingivoplasty, frenectomy, biopsy, treating, mucosal lesions, vaporization of dense fibrous tissue, debulking substantial soft tissue masses (because of shallow thermal necrosis zone) and coagulation after completion of surgery (a defocused beam is used to place a biologic bandage called 'eschar' on the wound surface).	Decontamination of cavity sites. Caries removal and cavity preparation. Removal of dentin and pulpal tissue (RCT). Bone removal. Tissue retraction for uncovering implants.

Table 20 - Laser wavelengths used in dentistry (*Cont'd.*) [184].

Laser	**Argon**	**Diode**	**Nd:YAG**	**Ho:YAG**	**CO_2**	**Erbium family (ErCr :YSGG, Er:YAG)**
Advantages	Enhanced physical properties, improved adhesion, reduced microleakage and less curing time (10 secs) compared to conventional curing light. Excellent haemostatic capabilities. No damage to the tooth structure during soft tissue procedures because of poor absorption into enamel and dentin.	Small, portable and compact unit. Excellent soft tissue surgical laser. However, haemostasis is not as rapid as with argon laser. Soft tissues surgeries can be performed in close proximity to enamel, dentin and cementum as these lasers are poorly absorbed by the tooth structure. Lowest priced lasers currently available. The 655 nm visible red diode excites fluorescence from a carious tooth which is reflected back into a detector in the unit that analyses and quantifies the degree of caries.	The free running pulsed mode allows the clinician to treat thin or fragile tissue with a greater safety margin of preventing heat build-up in the surrounding area. Allows for safe and precise soft tissue surgery adjacent to sound tooth structure as there is little interaction with the tooth structure. Pigmented surface carious lesions can be vaporized without removing the healthy sound enamel. Can penetrate several millimetres when used in a non-contact defocused mode, which can be used for procedures such as haemostasis, treatment of aphthous ulcers or pulpal analgesia.	Efficient tissue ablation at the surgical at the surgical site because of good absorption by water in the soft tissues. Optic fibre affords good access, precision and tactile feedback. Collateral thermal damage can be avoided because it is produced in a pulsed mode. The lasers absorbency by tooth structure is low, which allows tissue surgery in close proximity to enamel, dentin or cementum to proceed safely.	Precise and quick soft tissue vaporization in a non-contact mode without a need to touch the tissue is especially advantageous when treating movable oral structures such as tongue and floor of the mouth.´ Large lesions can be treated with a simple back and forth motion.	Painless procedure. Absence of vibration or high pitched noise experienced during the procedure. Provides the tissue interaction characteristics to perform effective RCT and bone removal. Can readily ablate soft tissues because of its high water content and the lasers affinity for water. A carious lesion in close proximity to the gingiva can be treated and the soft tissue recontoured with the same instrumentation. The non-interaction with precious metal and fused porcelain allows the practitioner to remove caries surrounding the restorations without any damage. Tissue retraction for uncovering implants is safe with these wavelengths because there is minimal heat transferred during the procedure.

A complete temperature graded profile is proposed in **Fig. 46** with different temperature ranges indicating different applications and morphological changes [184,188–190].

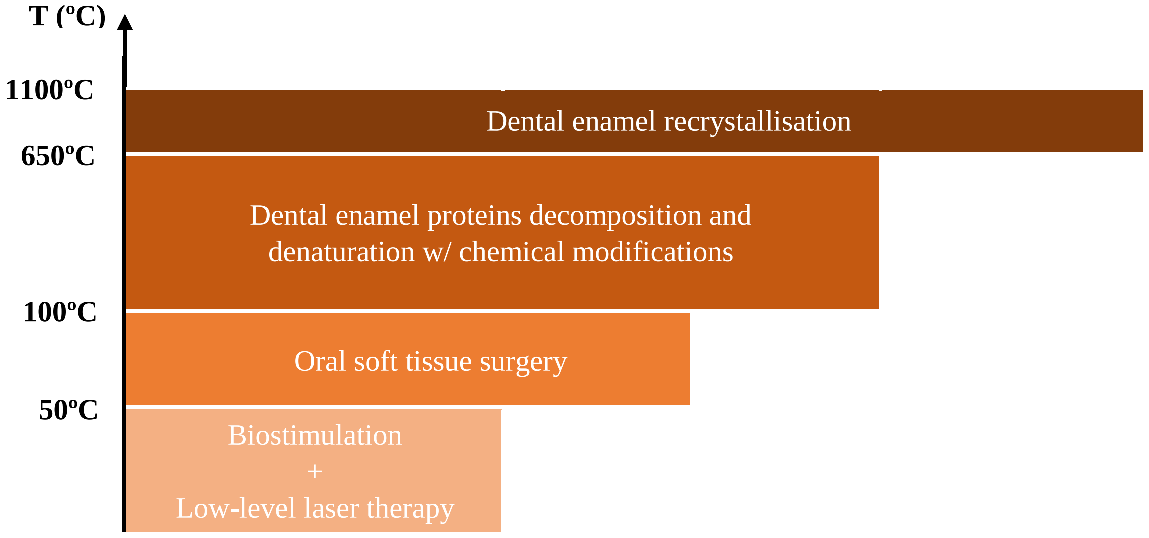


Fig. 46 - Temperature graded profile of oral soft and hard tissues.

In **Fig. 46** it is important to notice that with temperatures below 50ºC, lasers are applied for biostimulation and low-level laser therapy. Contrary to the high irradiation intensities verified for hard dental tissues, in these procedures the aim is to have fluency deliveries from 2 to 10 J/cm^2. Accordingly to Bhat [184] the values of fluency delivery will differ with the type of tissues irradiated: oral epithelium and gingival tissue, transosseous irradiation or extraoral muscle groups (**Fig. 47**). Analysing the utilised low-level lasers, helium-neons and infrared diode lasers with wavelengths ranging from 633 nm to 904 nm showed to be suitable for successful therapies, according to an earlier study from Willenborg [182] and more recently confirmed by Bhat [184] study. Microradiography and confocal laser scanning microscopy were already utilised for identification of possible enamel lesions by 1996 [191].

The application of this non-destructive tomographies combined with low-level laser techniques, reflected reduced inflammatory rates, less postoperative discomfort and improved quality of healed tissues [186].Furthermore, Doshi-Mehta and Bhad-Patil [190] concluded that low-level laser therapy increases the rate of orthodontic tooth movement by altering the biologic response without tooth anchorage modifications.

Laser	Wavelength
Helium-Neon	633 nm
Diode GaAs	820 nm
Diode GaAs	904 nm
Diode GaAIAs	780-890 nm
Diode InGaAIP	630-700 nm

BIOSTIMULATION
+
LOW-LEVEL LASER THERAPY

Tissue	Fluency
Oral epithelium and gingival tissue	2-3 J/cm^2
Transosseous irradiation	2-4 J/cm^2
Extra-oral muscle groups	6-10 J/cm^2

Advantages

- Reduced inflammation
- Less postoperative discomfort
- Improved tissue quality

Fig. 47 - Laser wavelengths and fluencies for advantageous purposes in biostimulation and low-level laser therapy (built based on data from [182,184,186]).

7.2. Orthodontic wires – mechanisms and structures

In dentistry, orthodontic wires appliances are a common method for tooth treatment and correction. Initially, continuous arch wires were utilised however, it was noticed that the force system applied did not differentiate active correction forces from reactive forces and so the outcomes were divergent from the initial planned procedure [192,193]. Consequently, the combination of segmented wire appliances improved dental correction results due to a more diversified manipulation and force system definition [194]. Additionally, it is important to refer that the geometric characteristics of the wire will also contribute to the force and moment interactions with tooth movement (**Fig. 48**).

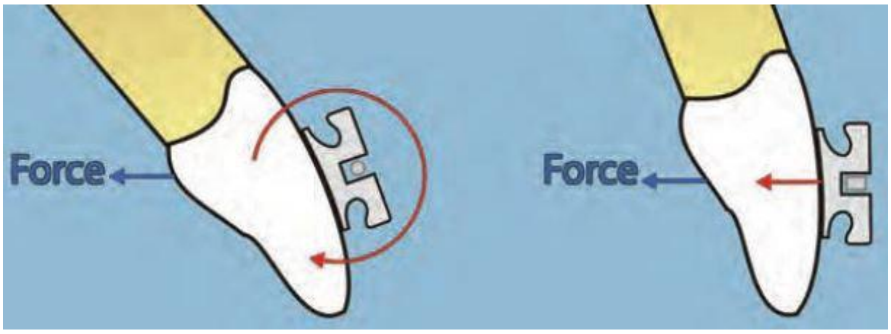


Fig. 48 - Comparison of rotation and translation tooth movements with different archwire geometries [194].

Naini and Gill [194] presents a table (**Table 21**) where the application of round or rectangular archwires considering the three types of bend possible in tooth correction, are summarised. However, previous studies from Kapila and Sachdeva [195], state that rectangular wires are desirable since they are better oriented in the bracket and so the force system created will interact in accurate directions allowing an improved control over tooth anchorage position.

Table 21 - Classification of orthodontic archwire bends. [194].

Type of bend	Archwire type required	Tooth movement generated
First-order bend (also termed 'in-out' or horizontal 'offset' bends; vertical step bends that do not alter the tooth's angulation are also in this category)	Round or rectangular stainless steel	Buccolingual offset of a tooth crown un the horizontal plane; or vertical translation of a crown without change in angulation.
Second-order bend (also termed 'tip bends' or 'angulation bends')	Round or rectangular stainless steel	Mesiodistal angulation of the tooth crown and/or root
Third-order bend (also termed 'torquing bends' or 'inclination bends')	Rectangular stainless steel or TMA (titanium-molybdenum alloy).	Buccolingual crown and/or root inclination.

According to literature, planning of tooth correction procedure is a fundamental process where orthodontic wire appliances can be custom-design to adapt a specific clinical situation. In this pre-treatment phase, evaluation and analysis of technical characteristics such as inter-bracket distances, wire curvature, direction of force activation relative to the wire curvature, bracket width and friction between the bracket and wire is necessary for optimisation of the developed appliances [194,195]. In this matter, Fiorelli *et al.* [193] developed the Dental Movement Analysis (DMA) software where force vectors were simulated considering the tooth centre of resistance with posterior visualisation of the pretended dental movements (**Fig. 49**). Another characteristic that will also influence the optimised force system is the welding points applied on segmented wires and single-tooth correction auxiliaries [192].

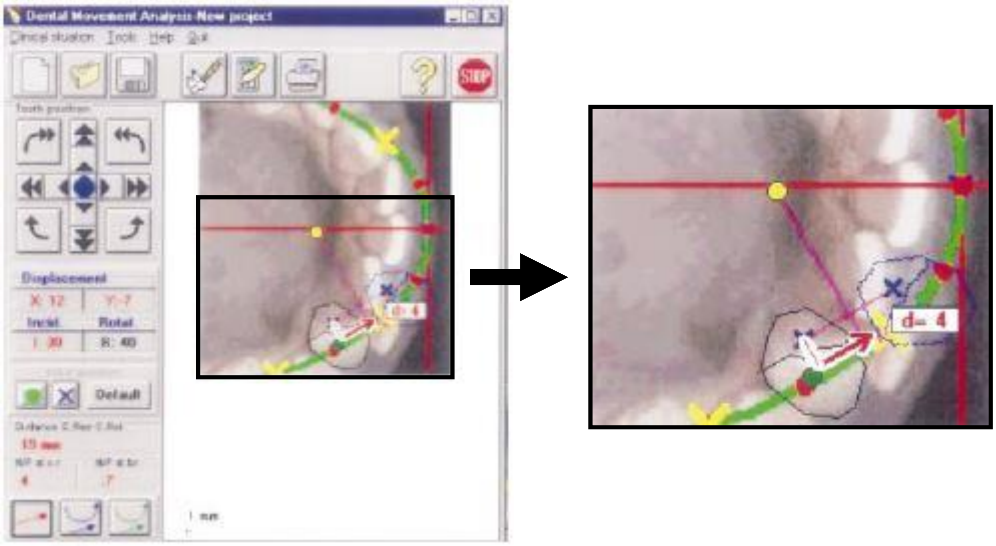


Fig. 49 - Dental Movement Analysis (DMA) software [193].

The importance of welding procedures in these type of orthodontic corrections is illustrated by **Fig. 50** where the specific welding point of different appliances generated the necessary force corresponding to previous calculations made with the DMA software [193].

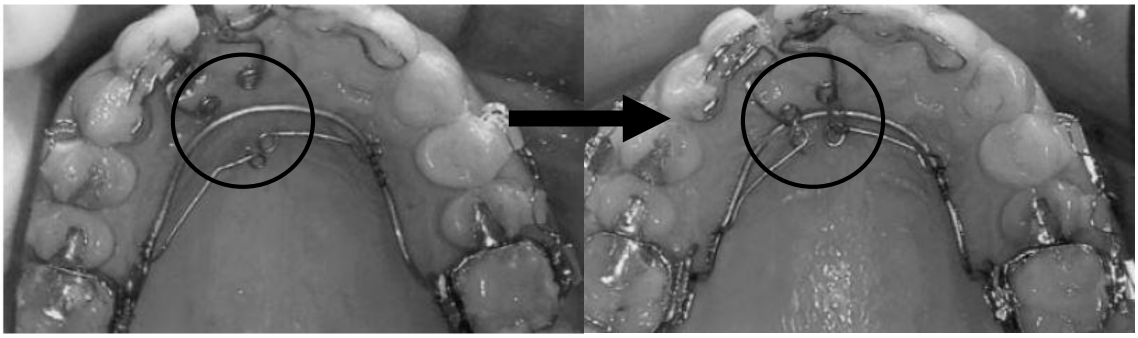


Fig. 50 - Weld between segmented archwires for correct force system application [193].

On the other hand, when observing the different stages of treatment with orthodontic wires, various auxiliaries can be applied to the main structure such as attachments, gable bends or closing loops. In the early 2000s, Cacciafesta and Melsen [192] presented an interesting study of rectangular loops application in orthodontic wires for single-tooth corrections. They demonstrated that different forces and moments resulting from the loop activation would be directly related with the angulation, inclination or rotation corrections, achieved with maximum control of tooth movement (**Fig. 51a**). Consolidation of posterior Fiorelli *et al.* [193] findings on the importance of welding was already herein verified with the position of the welding point in the orthodontic structure considered crucial to the achievement of the expected type of correction (**Fig. 51b**).

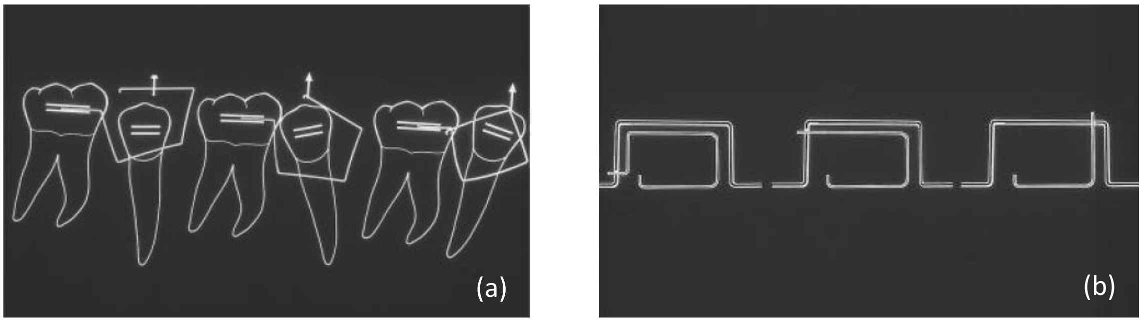


Fig. 51 – (a) Tooth movement and orientation accordingly to different force application in the loop. (b) Different weld spot localisations for the loop to achieve expected tooth movement [192].

7.2.1. Materials

Suitable material properties for orthodontic wires focus on a good springback (flexibility), low stiffness, good formability, biocompatibility, reduced surface friction and weldability [195,196]. To achieve an optimal combination of these properties it is necessary to analyse the evolution of the materials utilised in dental procedures. For this purpose, **Fig. 52** illustrates the chronologic appearance of materials such as stainless steel and titanium alloys, in this field [48,195–198].

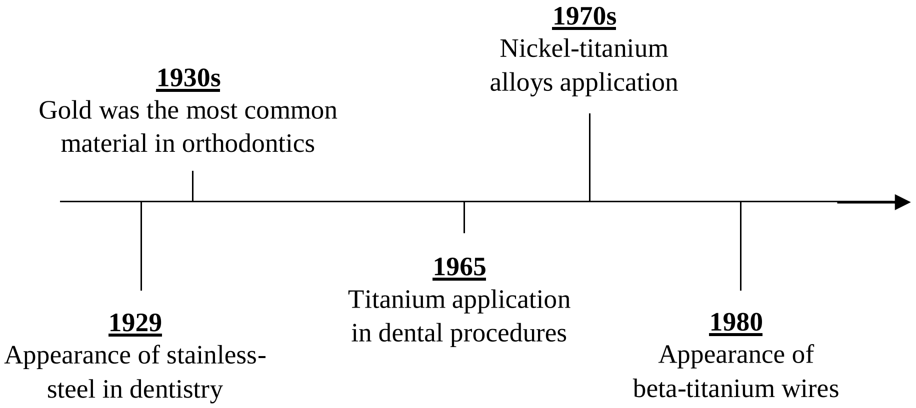


Fig. 52- Chronologic implementation of different materials in dentistry until 1980 (built based on data from [195-198]).

According to literature, the most common materials utilised in orthodontic wires are stainless steel, cobalt-chromium and titanium alloys such as nickel-titanium and beta-titanium alloys. Observing Kapila and Sachdeva [195] comparison of these materials for dental application (**Table 22**) it is possible to identify the beta-titanium wires as the most suitable due to their springback, formability, biocompatibility, corrosion resistance and weldability properties.

Table 22 - Comparison of some desirable clinical characteristics of orthodontic wires [195].

Wire	Springback	Stiffness	Formability	Stored energy	Biocompatibility and environment stability	Joinability	Friction
Stainless steel	Low	High	Good	Low	Good	Soldered Welded	Low
Cobalt-chromium	Low	High	Good	Low	Good	Soldered Welded	Low-moderate
Nickel-titanium	High	Low	Poor	High	--	Not joinable	Low-moderate
Beta-titanium	Average	Average	Good	Average	Good	Welded	High
Multistranded	High	Low	Poor	High	Good	Soldered Welded	Not known

Nevertheless, the segmented appliances previously mentioned allowed a diversified application of these materials in the different stages of tooth treatment. The application of different materials can actually improve the expected results due to the relation of material properties with desirable tooth movement [197,199]. Initial tooth alignment and levelling requires improved stored energy and springback properties since the active forces have greater impact on the wire at these early stages. Intermediate stages with single-tooth corrections require application of orthodontic auxiliaries therefore weldability is the main characteristic to consider. In the final stages of treatment, stiffness and formability of orthodontic wires are necessary for elimination of occlusal interferences and maintenance of tooth correction (**Table 23**).

Table 23 - Suitable materials, properties for different stages of orthodontic treatment.

Stage of treatment [195,196]		**Material** [196,198]	**Properties** [48,197]	**Purpose** [193,196]
Initial	Alignment Levelling	Titanium wires	Stored energy Springback	Active forces, initial tooth movement
Intermediate	Decomposition Incision inclination preparation	Beta-titanium	Springback Weldability	Auxiliaries loops and attachments needed
Final	Arch coordination Elimination of occlusal interferences	Stainless-steel Cobalt-chromium	Stiffness Formability	Final tooth correction and stability

7.2.2. Welding techniques

The joinability of different materials in orthodontics is an important characteristic to achieve tooth correction objectives. Soldering and welding are the most common techniques, being welding techniques mainly centred in infrared brazing (IB), electrical resistance welding (ERW) and laser welding (LW), accordingly to Iijima *et al.* [196,197] and Bertrand and Poulon-Quintin [48].

When comparing these three welding techniques, laser welding is the most suitable since precise and defined welds can be achieved with or without solder application and complications such as distortion can also be easily corrected due to the minimal effect on mechanical properties as formability [197]. Furthermore, with the adjustment of laser parameters (power, pulse duration, energy, shape, spot size, etc.) it is possible to increase corrosion resistance of the welding since vaporisation of alloying elements is prevented [48]. Bertrand and Poulon-Quintin [48] refers porosities and cracks as the main metallurgical effects present in laser welding and establishes an optimal range for pulse duration and power combinations where suitable welds can be obtained (**Fig. 53**).

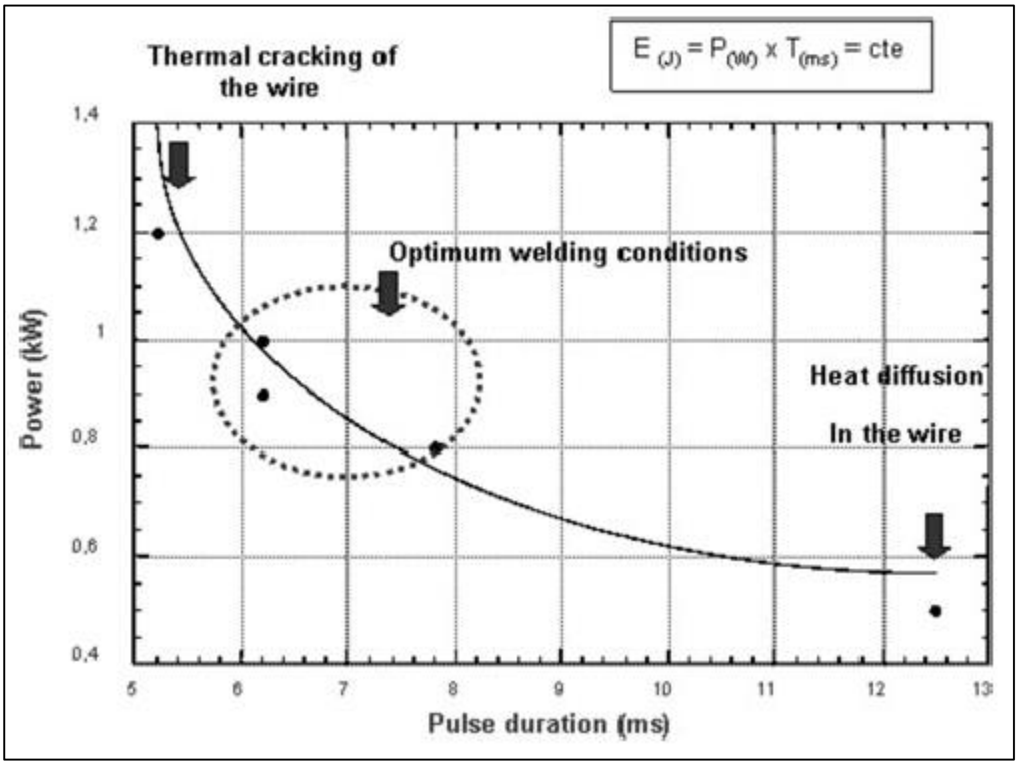


Fig. 53 - Adjustment of welding settings (power and pulse duration) for optimal conditions [48].

Observing **Fig. 53**, the optimum laser welding conditions are achieved with pulse durations and power settings between 6 to 8 milliseconds and 0.75 to 1.15 kilowatt, respectively. Two other regions can be identified in **Fig. 53**: thermal cracking and heat diffusion regions. The first is characterised with high power settings and short exposure times whereas the latter corresponds to longer exposure times and low power settings. Despite the advantageous characteristics of the laser welding technique, nickel-titanium alloys cannot be welded, as seen previously in **Table 22**.

Infrared brazing was initially introduced in orthodontics due to its easy manipulation and lower cost but increased heat-affected zones and possible oral toxicity due to solder corrosion, should be concern factors to consider [48,199]. On the other hand, electrical resistance welding is a technique where solder application is needed to join different materials which can result in decreased mechanical properties in the welded joint.

Alternatively to these welding techniques, a recent study by Matos *et al.* [200] presented the tungsten inert gas (TIG) welding technique combined with brazing welding for the joining of orthodontic wires, due to its quick and simple application. Consequence of an inert atmosphere, galvanic effects were absent from the weld.

In terms of corrosion resistance characteristics, another recent study by Zhang *et al.* [201] proposed a composite arch wire (CAW) made of nickel-titanium alloy, stainless-steel and a copper interlayer concluding that this type of wire presents a viable solution in the orthodontic field due to its biocompatibility and corrosion resistance.

The relations of welding techniques with the exposed materials for orthodontic applications is summarised in **Table 24**, presenting their advantages, drawbacks and suitable materials. An interesting investigation of welding materials for orthodontic applications is made by Matsunaga *et al.* [199] where the dissimilar weld of titanium based alloys with stainless-steel and cobalt-chromium alloys made possible the comparison between different welding techniques such as LW and ERW. Their results show that in terms of homogeneous welding of materials, laser welding presented better results with titanium alloys and electrical welding with stainless-steel and cobalt-chromium wires. Contrary to this, it was verified that in heterogeneous welding, maximum load at fracture and elongation was achieved by electrical resistance welding technique.

Table 24 - Welding techniques advantages, drawbacks and application in suitable materials.

Welding technique [196,197]	**Advantages** [48,199]	**Disadvantages** [48,199]	**Materials** [195,196,198]
Infrared Brazing (IB)	Easy to use Less expensive than LW	Possible oral toxicity Increased HAZ effect Brittleness in solder joint	β-Ti alloys Ni-Cr alloys
Electrical Resistance Welding (ERW)	High values for maximum load at fracture and elongation with welding of heterogeneous materials	Solder needed	Stainless-steel Co-Cr alloys Co-Cr-Ni alloys
Laser Welding (LW)	Minimal HAZ effect Welding with or without solder Higher joint strengths	Higher cost comparing with IB and ERW Not suitable for nickel-titanium alloys	Titanium alloys Stainless-steel β-Ti alloys Co-Cr alloys Co-Cr-Ni alloys

7.3. Prosthodontics

In the prosthodontic field, according to Bidra [202], there is a variety of treatment options to consider for prosthesis integration. From the options presented in **Table 25**, it is important to refer that implant-supported overdentures have lower cost associated due to less invasive and expensive surgical procedures [203]. Additionally, the presented options must be considered accordingly to the surgical factors that will determine the best solution for prosthetic application (**Table 25**).

Table 25 - Surgical factors in prosthodontics (built based on data from [202,203]).

Surgical factors	Surgical guides with preservation of the gingiva	
	Bone quality	
	Choice of implant system	
	Number of implants	
	Three-dimensional position and angulation	
	Implant dimension and parallelism	
Prosthesis integration options	Single-screw retained	Metal structure w/ individually cemented crowns
	Removable overdenture	Individual attachments
		Support bar(s)
	Screw-retained fixed prosthesis	Metal-resin or metal-porcelain materials
	Cemented fixed prosthesis	

Paek *et al.* [50] refers the importance of space in the oral cavity for orthodontic applications with the addition of utilising laser welding technique to correct another crucial surgical factor, the angulation of implant abutments which is also one of the most difficult problems to overcome in implant-supported prosthesis. In this matter, Bidra [202] had already corrected abutments angulation with a 17° bending of plastic tubes (**Fig. 54**) with an excellent passive fit of the metal bar over implants applying the same technique (point-laser welding).

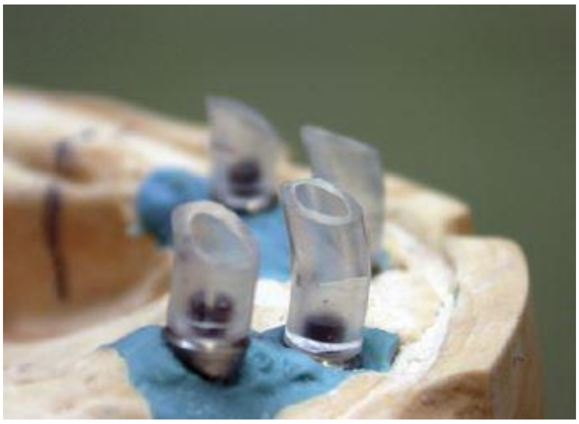


Fig. 54 - Plastic tubes bending to change the screw access channel in the metal bar [202].

The biological interaction between bone and implant structures is of utmost importance since it determines the adaptability of involved tissues and dental structure, to the applied mechanical forces from the prosthetic implant. In cases where existing dentition cannot provide sufficient structural stability, the anchorage of previously mentioned orthodontic appliances has to be made through enosseous oral implants [204].

Therefore, the relation between functional loading and passive fit will influence the osseointegration success. If passive fit between framework and abutments is optimised, the amount of stress and strain is limited in bone-implant surfaces. Otherwise, mechanical and biological drawbacks can interfere, such as screw loosening, bar deformation, fatigue or fracture and bone loss near the implant anchorage [203,205].

In the early 2000s, problems with possible cold welding properties in cone-screws (associated with screw-loosening complications), due to torque application, were investigated by Norton [206] concluding that despite higher clinical stability, these implants were still retrievable. By 2004, Longoni *et al.* [207] achieved precise fit of titanium components with the combined application of luting sequence and laser welding technique.

Other techniques for prosthetic misfit improvements can also be considered such as computer controlled milling or casting of frameworks. Similar to the previously demonstrated in orthodontic wire appliances, computer-assisted implantology is well demonstrated in Albiero and Benato [205] study. Thus, with preoperative planning (**Fig. 55**), surgical guides such as mechanical tolerance between drill and drilled holes is improved, implant placement is equally optimised and damage to surrounding structures such as nerves can be effectively prevented [186,205].

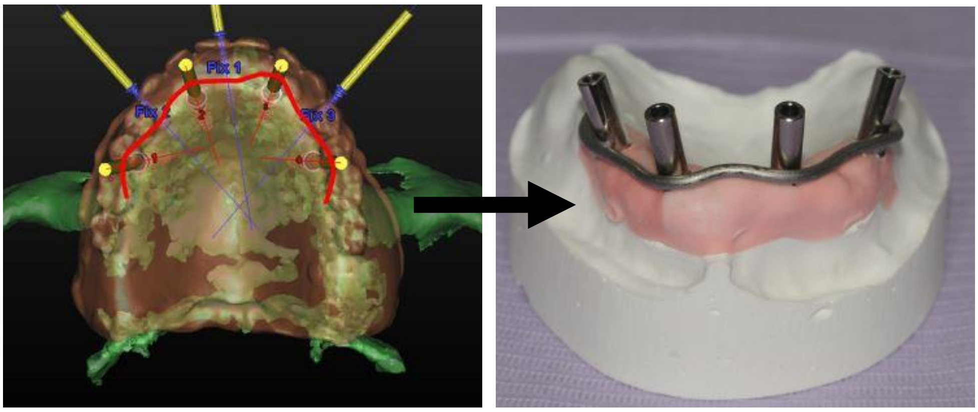


Fig. 55 - Computer-assisted implantology and resulted framework [205].

7.3.1. Intraoral welding procedure

Intraoral welding technique was first introduced in 1982 [177], with the application of electrical resistance welding in titanium components. According to Albiero and Benato [205], by 2006 studies of intraoral welding of titanium bars in implant abutments were successful procedures to create suitable mechanical structural reinforcements. Degidi *et al.* [208] verified that intraoral welding technique is appropriated for implants applied with low intensity torque values, concluding that it limited micro-movements and consequently beneficiated osseointegration. Welding of additional bars, as illustrated in **Fig. 56**, also increases the strength of the framework [208].

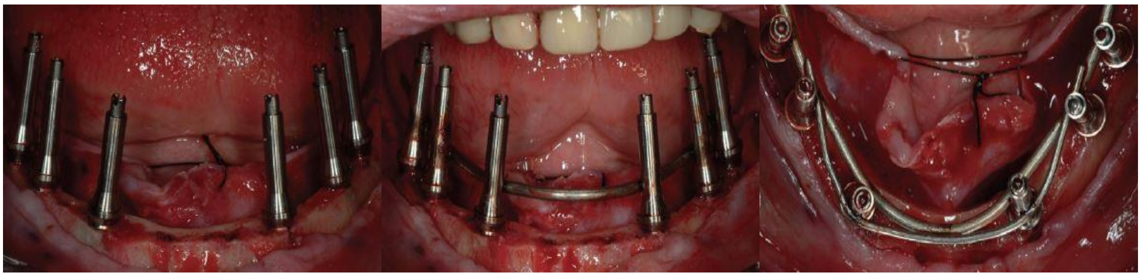


Fig. 56 - Intraorally welded framework with primary and secondary bars [208].

According to literature [205,208], intraoral welding is a technique where shaping and welding of the framework on the provisional abutments can be performed with minimal or absent fracture of provisional restoration. Furthermore, immediate load can be applied and it allows simplified application of fixed temporary prosthesis.

Despite these advantageous characteristics, thermal damage and heat dissipation are still concerns in surgical welding prosthodontic procedures [209,210]. In Degidi *et al.* [209] study the highest temperature measurement with thermal infrared imaging, never surpassed 39ºC which is below the considered temperature for bone damage (56ºC). They also mention that it is possible to control heat dissipation in welded points by maintaining or removing the welding system copper clamps, utilizing long pin screws and by changing the type of screw connections.

More recently, studies have been reported about the application of welding technologies in prosthodontics with Mohunta *et al.* [211] replacing worn overdenture abutments using a laser welding system consequently achieving the reduction of cost and operative time (**Fig. 57a**). In 2015, laser welding was applied in combination with an argon flux, by Paek *et al.* [50], to join a milled head part of C-implant to a customised lingual part for correct esthetical fitting of a dental cap (**Fig. 57b**). One year later, Ferraris *et al.* [210] reported a new technique with electrical resistance welding in which a circumferential pulsing machine was created to diminish the weakness of the intraoral joints and with two electric impulses a uniform weld is executed with no inclusions, porosities or alterations in the joining area. Additionally, the un-oxidised circumferential welds also showed potential for resistance of possible bacterial corrosion (**Fig. 57c**).

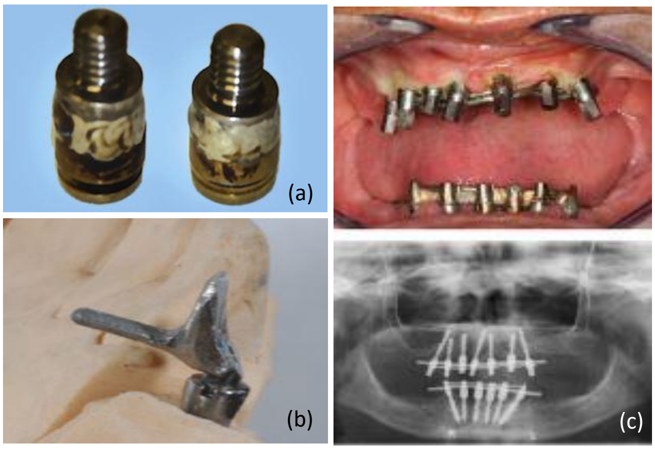


Fig. 57 - (a) Repaired worn overdenture abutments with laser welding [211]. (b) 2-piece orthodontic C-implant with laser welded customised coping [50]. (c) Intraoral welding result with electrical resistance welding technique [210].

It is important to refer that although titanium is the most common material utilised in prosthesis procedures, dental implants have been made from a multitude of materials such as platinum, silver, steel, cobalt alloys, alumina, niobium, zirconia and calcium phosphate compounds, accordingly to the recent study of Zandparsa [186]. From these materials, the suitable alternatives to titanium implants are ceramics and zirconia implants, due to their mechanical properties, low-thermal and electrical conductivity, biocompatibility and esthetical properties (colour), as well [186].

7.4. Mandibular reconstruction

Mandibular fractures were primarily restored through free tissue transfers with microvascular anastomosis, i.e., vascularised bone grafts [212]. According to Cobetto *et al.* [213], the evolution of mandibular surgery was confirmed in the 1970s with the introduction of titanium and biodegradable plates. Non-vascularised bone grafts enhanced maxillomandibular fixation surgeries with less intra-operative time, less sensitivity to the technique and optimal reconstruction for posterior dental implant prosthetics [212].

By 1983, Cobetto *et al.* [213] had reviewed 120 cases where titanium plates and meshes were applied for mandibular reconstruction concluding the feasibility of such procedure. More recently, Yamashita *et al.* [49] demonstrated how titanium meshes can still be an excellent method for mandibular structures, improving pre-operative planning with the utilisation of computed tomography (CT) for accurate and precise three-dimensional simulation of the mesh application. Additionally, with the laser welding technique, Yamashita *et al.* [49] was able to reinforce the mesh loaded areas and process complex bends (**Fig. 58**).

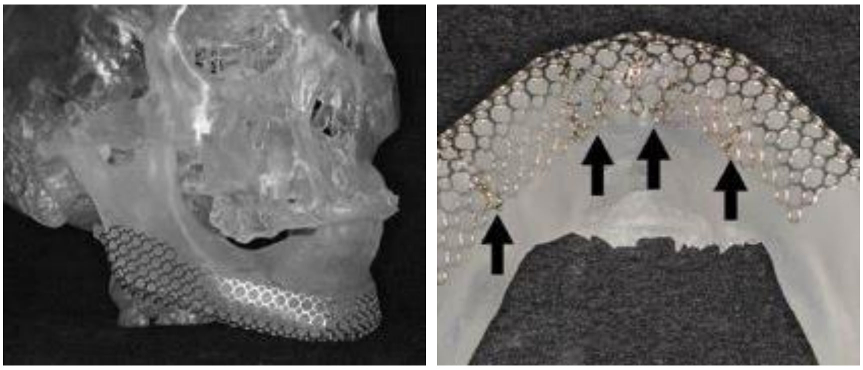


Fig. 58 - Reinforced titanium mesh sheet shaped to match the craniofacial bone model (arrows: areas reinforced by laser welding) [49].

The innovation of biodegradable plates and screws was made with the application of SonicWeld Rx in SonicPins Rx for fixation of resorbable meshes designated by Resorb-X [26,212,214]. In this revolutionary technique an ultrasound activated sonic electrode is utilised (**Fig. 59a**) for the insertion of pins with 4 to 5 mm of length and 2.1 mm diameter (**Fig. 59b**). The fixation of the resorbable mesh is achieved by shaping it in a water bath at approximately 70ºC with final disposition being made in the patient mandible. According to Meara *et al.* [214], the welding of the pins produces a maximum temperature of 33.1ºC, inferior to the previously mentioned 56ºC for bone necrosis making this technique suitable for the pretended purpose.

(a) (b)

Fig. 59 - (a) Sonotrode handpiece. (b) Pin welded to plate with penetration into surrounding bone [214].

Furthermore, **Table 26** lists the advantages of this method over standard methods to date, such as titanium and biodegradable plates and screws for fixation and healing of mandibular fractures. Confirming the suitability and adaptation of this innovative technique, El-Saadany *et al.* [26] recently reported that it is preferable for mandibular restorations in paediatric patients due to their mixed dentition and bone structure development, which can become a problem for fixed plates and screw attachments.

Table 26- Comparison between biodegradable plates, titanium mesh plates and Resorb-X mesh with SonicPins.

	Advantages	**Drawbacks**
Biodegradable plates with screws [26,212,214]	Removal not required Reduced sensitivity when compared w/ titanium applications	Tapping of screws necessary Inferior mechanical properties when compared w/ titanium applications
Titanium mesh plates with screws [49,213]	Superior mechanical properties when compared w/ biodegradable plates Combination w/ LW technique allows complex bends and strengthen loaded areas in the mesh	Patient hypersensitivity Screw or plate migration Hardware infection Growth restriction
Resorb-X mesh with SonicPins (SonicWeld Rx) [26,212,214]	No thermal sensitivity Easy application w/ no growth dentition limitations Removal not required Less operative time due to no tapping of screws required	N.R.

NR - Non-referred.

7.5. Main remarks

- Oral and maxillofacial surgeries can be performed with a multitude of lasers due to their characteristics and clinical applicability. In dental hard tissues, laser irradiation intensity and wavelength are important characteristics for successfully healing and recrystallisation processes. Biostimulation and low-level laser therapies are successfully achieved with proper fluency and wavelength settings.
- Combination of segmented wire applications improve dental correction results. With the application of DMA software and laser welding, in the joining of different force systems appliances, ensures final dental optimisation.
- Suitable material properties for orthodontic wires focus on a good flexibility, low stiffness, good formability, biocompatibility, reduced surface friction and weldability. Beta-titanium wires are the most suitable mainly due to mechanical, corrosion and weldability properties over other materials such as nickel-titanium alloys that cannot be welded.
- The most common welding techniques utilized in orthodontic applications are infrared brazing, electrical resistance welding and laser welding. Despite its associated higher cost, LW employs a wide variety of alloys with advantageous effects such as the option of solder application and minimal HAZ.
- In prosthodontics, precise fit of components with the combined application of luting sequence and laser welding technique has been confirmed and improved prosthodontics post-operative results.
- Intraoral welding technique is appropriated for implants applied with low intensity torque values, and limits micro-movements consequently beneficiating osseointegration. More recently, in mandibular fractures restoration, ultrasonic welding technique known as SonicWeld Rx has demonstrated improved results over titanium mesh plates.
- Contrary to the previous chapters, it was necessary to approach the dentistry field not only through the understanding of tissue welding process but also with the consideration of the importance of welding techniques in orthodontic and prosthodontic materials with specific weld spot locations to assure the optimised results previewed with computer-assisted implantology softwares.
- The overview of this chapter indicates that throughout the years and with the development of new dental technology tools, standard and innovative welding techniques in oral and maxillofacial procedures are a viable choice for the achievement of excellent and improved overall results.

8. DISCUSSION

Improvement of human tissue regeneration has always been a frontline goal to the medical community. With preventive and reconstructive medicine, human life expectancy grows every day. The continuous and intensive research made on innovative technologies and medical techniques allowed medical fields such as ophthalmology, angiology, neurology, urology, otolaryngology or dentistry, to excel conventional practices with safer, efficient, faster and reliable surgical interventions and therapies procedures.

Taking in consideration the content of the previous chapters, it is clear that each one of them has particularities when it comes to tissue regeneration with welding technologies. Nevertheless, it is also important to notice that from the techniques herein approached, laser welding presented a core position among them (**Table 27**).

Table 27 - Studied welding techniques in the different medical fields.

		Welding techniques
Studied medical fields	**Angiology and Neurology**	**Laser welding** CO_2, Nd:YAG, Argon, Diode, KTP, Intraluminal light source **Alternative** PTB, HFEW
	Ophthalmology	**Laser welding** CO_2, Nd:YAG, Argon, Diode, HF **Alternative** HFEW
	Dentistry	**Oral laser welding** CO_2, Nd:YAG, Argon, Diode, HF, Erbium **Orthodontic and prosthodontic** IB, ERW, LW, TIG with brazing **Mandibular reconstruction** SonicWeld (Ultrasound welding biodegradable pins)
	Otolaryngology	**Laser welding** CO_2, Nd:YAG, KTP **Alternative** TWT, APC, MCD, BCD, Radiofrequency thermoablation
	Urology	**Laser welding** CO_2, Nd:YAG, Argon, Diode, KTP, Ho:YAG **Alternative** PTB

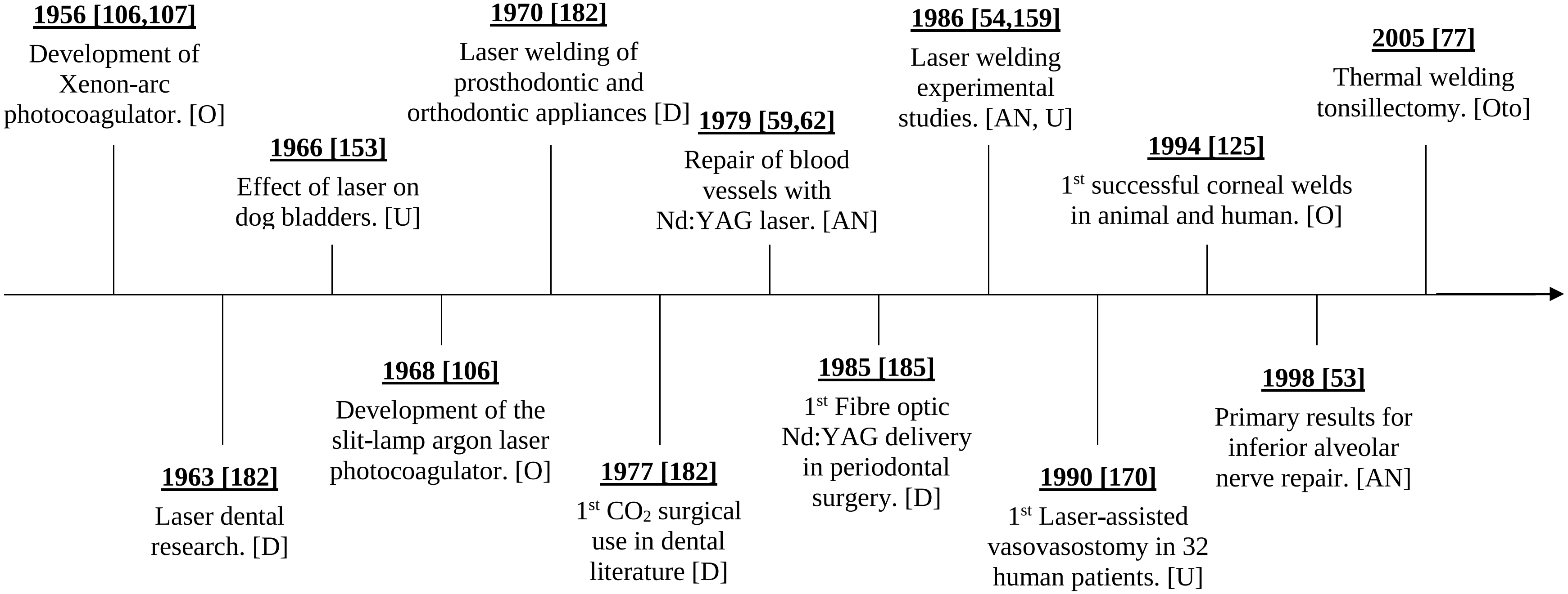
From an individual analysis of each chapter, the breakthrough milestones achieved with the evolution of such techniques were mostly verified in the XX century, although in the otolaryngology field, thermal welding was only considered by 2005. A global chronologic overview of these milestones is presented in **Fig. 60**.

Through the conducted literature research, it was observed that laser welding has a relevant core position in the health sector with an outstanding impact on the surgical procedures from many medical areas. Laser welding surgeries presented many advantages, such as non-foreign body reactions, absence of aneurysms, and reduced operative times with high recovery rates. However, despite the sutureless nature of the process, complementary sutures have been applied as a support of the procedure success. It was also verified that medical experience and the associated cost of such procedure, may limit its implementation in hospitals and clinics. Demonstration of the cost-weight analysis in welding surgery decision is exposed on thermal welding tonsillectomy instrumentation devices (**4.1 - Techniques and instrumentation**) with cost ranges rising from 148€ to 400€, compared to the 12€ cost of other techniques instrumentation devices such as electrocautery (EC).

In terms of the welding process characterisation, many studies suggested that the tissue biologic thermal denaturation of collagen fibrins was the main cause for tissue bonding links. Various thermal profiles were carefully studied for the application of laser welding in the different human tissues, being possible to assume that the average temperature for the achievement of a successful weld is located between 50ºC and 100ºC. However, when analysing this range of temperature, differentiations based on the medical field application were observed and can be clearly identified in **Fig. 61**. For example, in urology, literature research implies that optimal welds are mainly achieved in a narrower range from 65ºC to 70ºC. On the other hand, for vascular and nerve procedures, suitable weld temperatures do not arise the 65ºC, for protein denaturation. Complete corneal collagen denaturation is verified in higher temperatures from 76ºC to 100ºC. These divergent variations in different human tissues were only possible to be identified due to the XX century exponential growth of this technique, which beneficiated two aspects of extreme importance when it comes to laser welding application: thermal damage and welded tissue end point.

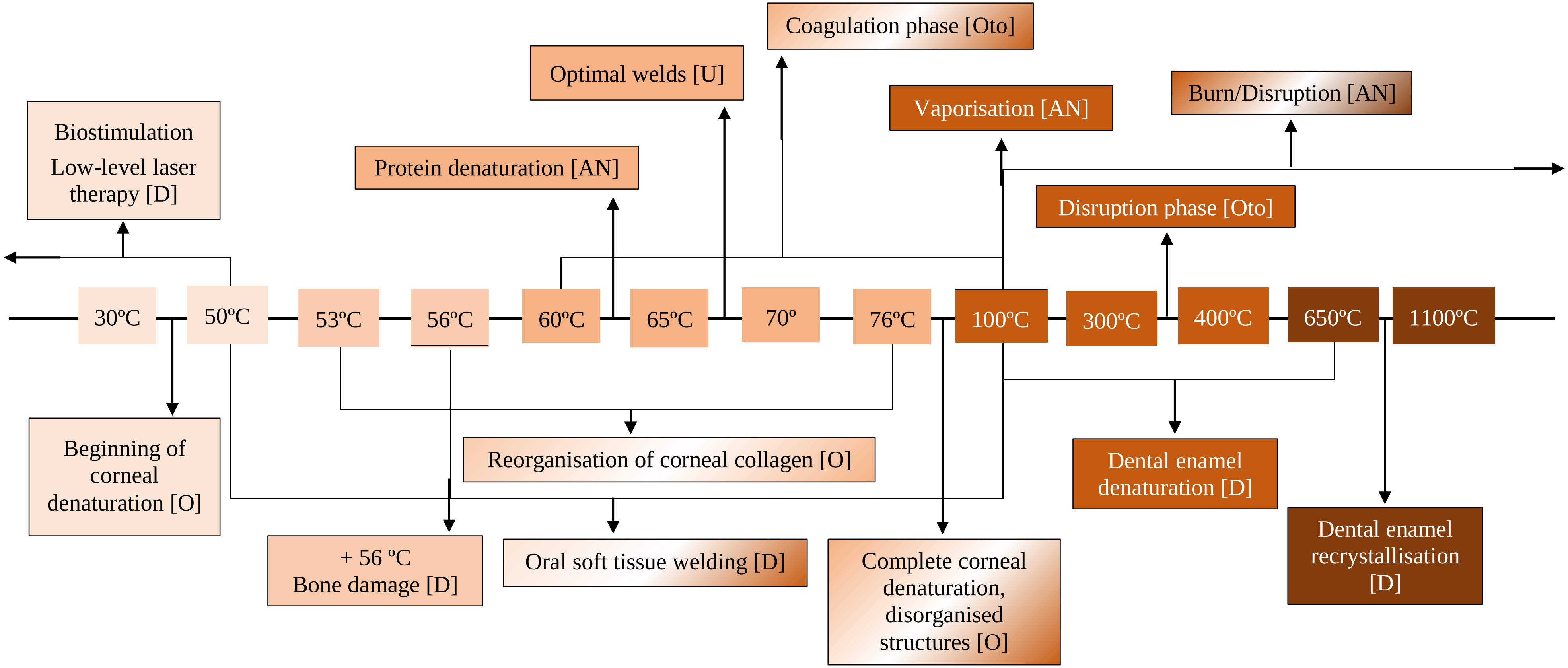
Thermal damage associated with laser welding is one of the laser-tissue interactions drawbacks that most concerns medical practitioners. Thermal damage from laser welding applications may induce permanent consequences in patients if not correctly minimised. As previously described, in ophthalmology (**5.1 - Ocular laser-tissue interaction**), thermal degeneration of ocular tissues can coagulate the cornea and consequently alter its curvature resulting in aggravated vision problems. When it comes to dentistry (**7.1 - Oral tissues, lasers and laser welding technique**), oral soft tissue thermal application must consider the protection of bone and teeth structures, so that if temperatures above 56ºC are applied (**Fig. 61**), they do not considerably damage these structures or escalate to a bone loss scenario.

The intensive studies, in this matter, were crucial for the standardisation of the optimal laser parameters adaptation to different types of surgery. Accurate setting of technical parameters such as suitable laser type, laser depth penetration, exposure time, suitable wavelengths compatibility and energy fluencies, has an important role in diminishing thermal degeneration of healthy surrounding tissues. This way, the development of temperature-controlled feedback systems along with simulation programs for the prediction of weld energy propagation and for the understanding of tissue healing process (MIAM), have enabled the reduction of this concern with such demanding accuracy. Additionally, application of cooling solutions, biologic solder solutions, bonding materials and laser-activated dyes have also contributed to reduce thermal damage while increasing the bonding strength of welds (**Fig. 62**).



[AN] - Angiology and Neurology; **[D]** - Dentistry; **[O] -** Ophthalmology; **[Oto]** – Otolaryngology; **[U] -** Urology;

Fig. 60 - Global chronologic overview of welding technologies early milestones in health sector.



[AN] - Angiology and Neurology; **[D]** – Dentistry; **[O]** **-** Ophthalmology; **[Oto]** – Otolaryngology; **[U]** **-** Urology;

Fig. 61 - Temperature biological modifications in welding procedures for different medical areas.

These external improvements also aided medical practitioners to noticeably identify the welded tissue end point without requiring, like in early years, visual identification scores with the different tissue appearances such as caramelisation, whitening, shrinkage, etc. (**3 - ANGIOLOGY AND NEUROLOGY**).

When observing the thermal damage topic across the chapters exposed, it is evident that such optimisation has had great improvements not only with external auxiliaries but also with the innovation of the laser welding technique to newly forms of tissue bonding that do not recur to thermal biologic modifications. The absence of thermal damage in the tissue bonding process was only achieved with the photochemical tissue bonding (PTB) technique and its specific dyes such as Rose Bengal or Riboflavin-5-phosphate.

Despite the strong presence of laser welding in tissue regeneration, other welding techniques also proved to be excellent suitable alternatives. Techniques such as high frequency electrosurgical welding (HFEW), the ligasure thermal welding tonsillectomy or even the SonicWeld Rx technique for mandibular reconstructions, demonstrate the versatility of welding technologies that can be applied with successful results in various medical areas.

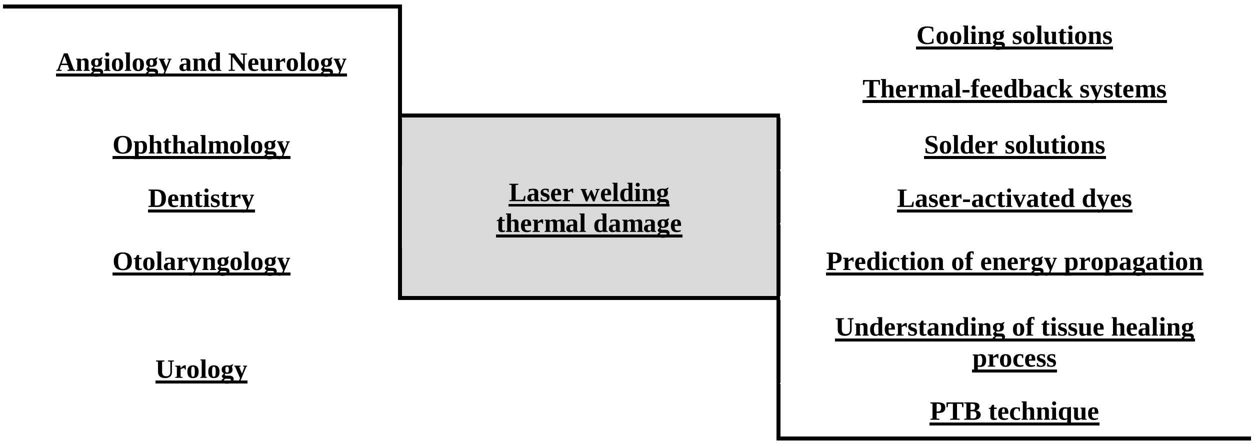


Fig. 62 - Thermal damage solutions for different medical areas.

From the conducted literature research, it is assumed that even though these alternative welding technologies presented great suitability for clinical practice with good results, they still have some limitations. These limitations are mostly evident in tonsillectomy thermal welding and in HFEW techniques since SonicWeld Rx has shown to be a technique with significant improvements in mandibular restoration with advantageous features over titanium mesh plates, such as absence of thermal sensitivity, less operative time and unnecessary removal of the biodegradable Resorb-X mesh. Nevertheless, the TWT and HFEW techniques did not shown statistically significant results when compared to other techniques as it was demonstrated, for example, in otolaryngology post-morbidity results (**4.2.1 - Operative and post-morbidity parameters**).

It is relevant to outline that the evolution, whether in the procedure itself or in instrumentation devices, of welding technologies still have a great impact in the health sector. Technology advances are constantly emerging and with that, welding techniques will be upgraded to achieve the perfect regeneration procedure, adapted to any human injury or disease. When analysing welding applications in medicine, the main breakthroughs were made in the late XX century and beginning of the XXI century. However, these breakthroughs were of extreme importance for the solid knowledge acquired in this field that allowed to the aforementioned innovative welding techniques to emerge. In this matter, literature research has also demonstrated that with the inclusion of nanotechnologies, enhanced robotics and image-processing, the improvement of welding technologies in tissue regeneration, prosthesis bio-integration, as well as treatment of chronic diseases have already been achieved with significant results. The scientific investigations that have been made and the continuous exploration of new clinical breakthroughs with such technologies, is definitely encouraging for the medicine related communities.

9. CONCLUSIONS AND SUGGESTIONS FOR FUTURE DEVELOPMENTS

The present section of the document intends to conclude about the research exposed and to identify new possible directions for future developments of welding technologies in the health sector.

9.1. Conclusions

New and innovative wound healing techniques have always been under development for the improvement of the human body regeneration. From the work presented it is possible to state that welding technologies have an important role in the remodelling of biologic tissues, specifically the laser welding technique. Nevertheless, other welding technologies have also been clinically applied with successful results such as ultrasound welding (SonicWeld Rx) or high frequency electrical welding (HFEW).

Across the medical fields studied, welding of soft tissues has protein denaturation of collagen fibres as the common denominator of the process characterization for the achievement of successful welds. The application of welding technologies in human tissue arises the problem of associated thermal damage and its minimisation or absence from the process is crucial for tissue regeneration.

Additionally, the development of new image-processing techniques, integration of robotics and nanotechnology transformed biologic welding procedures in more efficient and safer intra-operative and post-operative procedures.

The review of this topic consolidated and exposed, for any scientific area practitioner, the main implications of welding techniques within the regenerative surgeries and demonstrated how their chronologic evolutions led the field of wound healing to embrace emerging medicine fields, such as nanomedicine, as part of revolutionary personalised new tissue biologic designs.

Although most of the studies found through the conducted literature research were experimental-based, it is still necessary the investment in more long-term clinical trials with welding technologies, turning them a frontline choice for reconstructive procedures with reduced costs and wider medical acceptance.

9.2. Suggestions for future developments

The bridge of the technological world and medicine is an interesting and very relevant link for the present and future of human evolution. Whether in curing malignant diseases or upgrading human body parts/tissues, this type of commutability between different scientific fields will never cease to be crucial for the better understanding of newly processed information of a particular field of study.

Future developments of welding technologies may be taken in new directions through nanomedicine, three-dimensional reconstructive processes or even with the integration of regeneration surgery related artificial intelligent robotic systems. Nevertheless, the importance of the work here presented arises as these new paths are being discovered by the scientific community since without a full understanding of the relevant welding technology data, it is not possible to comprehend and achieve the so desirable medicine breakthrough results with those remarkable technological advancements.

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