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CICLO XXXV

BRAIN RETRACTION:

*dynamic-mechanical characterization of brain tissue
and development of novel devices*

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*Alla mia famiglia
e a chi voglia bene*

“Il nostro giocattolo più grande è il cervello...”

(Charlie Chaplin)

INDEX

<u>ABSTRACT</u>	p 1
<u>1. HUMAN BRAIN, STRUCTURE AND FUNCTIONS</u>	p 2
1.1 INTRODUCTION TO THE NERVOUS SYSTEM	
1.2 THE BRAIN	
1.3 ANATOMIC STRUCTURE	
1.4 NEURONS AND SIGNAL TRANSMISSION	
1.5 DENDRITES AND SYNAPSES	
<u>2. NEUROSURGICAL OPERATION</u>	p 6
2.1 HISTORY OF NEUROSURGERY	
2.2 CRANIOTOMY	
<u>3 HISTORY OF BRAIN RETRACTION</u>	p 8
3.1 STATE OF ART	
3.2 BRAIN RETRACTION INJURIES	
3.3 INTERMITTENT RETRACTION	
<u>4. LIMITS OF ACTUALLY TECHNOLOGY SOLUTIONS</u>	p 22
<u>5. MECHANICAL BEHAVIOUR OF BRAIN</u>	p 24
5.1 HOMOGENEOUS AND ISOTROPIC LINEAR ELASTIC BOND	
5.2 VISCOELASTICITY	
5.3 DYNAMIC MECHANICAL BRAIN BEHAVIOUR	
<u>6. DESIGN OF OUR INSTRUMENT</u>	p 30
6.1 OBJECTIVE	
6.2 MATHERIAL	
6.3 GEOMETRY	
6.4 SIMULATED GEOMETRY	
6.5 FEM ANALYSIS	
6.6 SIMULATIONS	
6.7 FEM ANALYSIS WITH BRAIN MODEL	

<u>7. MEASURES</u>	p 47
7.1 PIEZORESISTIVE SENSORS	
7.2 MISURE SYSTEM	
7.3 UPSUM HYBRIDE SYMULATOR SYSTEM	
7.4 TESTS PROCEDURES	
<u>8. LABORATORY TEST OF OUR INSTRUMENT</u>	p 50
8.1 RETRACTION TESTS	
8.2 SIMULATOR TESTS	
8.3 SPECIMEN TESTS	
<u>9. OUR DEVICES</u>	p 66
9.1 TRANSPARENT SPATULA	
9.2 CHAMBER	
<u>10. ANIMAL STUDY PHASE</u>	p 81
10.1 MINISTRY OF HEALTH APPROVAL: legislative decree March 4th, 2014, n. 26	
10.2 METHODOLOGY AND TECHNIQUE OF THE EXPERIMENT	
10.3 DECEASED SUINE PHASE	
<u>11. ADDITIONAL ACTIVITIES: ROBOT ASSISTANT FOR BRAIN SURGERY</u> p	91
11.1 General Working Principle	
11.2 Algorithm Description	
11.3 Experimental Results	
<u>12. CONCLUSIONS AND FUTURE PERSPECTIVES</u>	p 94
BIBLIOGRAPHY	p 96

ABSTRACT

Background. La retrazione cerebrale svolge un ruolo importante nella chirurgia cranica, ma i problemi che possono derivare da un'eccessiva retrazione non sono trascurabili. Il principale limite all'uso dei divaricatori cerebrali è la loro elevata possibilità di danno del parenchima: questo diventa particolarmente evidente negli interventi di tante ore che richiedono una retrazione di lunga durata. Possibili lesioni da retrazione cerebrale possono includere contusioni, ematomi ed emorragie che possono anche influenzare l'outcome del paziente.

Obiettivi del progetto. Il primo nostro obiettivo era quello di studiare gli strumenti attualmente presenti per la retrazione cerebrale analizzandone vantaggi e svantaggi. Successivamente, l'obiettivo principale era creare un nuovo strumento di retrazione cerebrale e convalidarne l'uso nella chirurgia cranica. Un altro obiettivo era quello di sfruttare la visione endoscopica anche nella chirurgia transcranica progettando camere di lavoro perfettamente adatte per introdurre facilmente l'endoscopio fornendo al contempo una retrazione sicura per il cervello circostante. Per raggiungere questi risultati è stato quindi necessario condurre un accurato studio in fase preclinica con la collaborazione di un team multidisciplinare.

Attività di ricerca e novità del progetto. L'attento studio di questo argomento, i test eseguiti in laboratorio di anatomia e di ingegneria, hanno permesso di creare nuovi strumenti tecnologici con molti vantaggi in campo neurochirurgico. La caratterizzazione meccanica dinamica del cervello permette di predire il comportamento meccanico del cervello umano sano e malato potendo anche prevedere ed eventualmente evitare complicanze per i pazienti. Grazie al progresso tecnologico nel campo della neurochirurgia, oggi la necessità di comprendere la correlazione tra la struttura del materiale e le relative proprietà viscoelastiche sta diventando sempre più cruciale anche al fine di sviluppare linee guida progettuali per la prossima generazione di biomateriali, per abbinare tessuti ed extra meccanica della matrice cellulare per modelli tissutali in vitro e applicazioni nella medicina rigenerativa.

Conclusioni e prospettive future. La conoscenza del comportamento del parenchima cerebrale in risposta ad una forza di compressione è quindi importante per comprendere i meccanismi alla base del danno, le soglie pericolose e quindi la possibile prevenzione delle complicanze cerebrali. Quest'ultimo aspetto è stato fondamentale per poter realizzare nuovi strumenti chirurgici "intelligenti" che operino in sicurezza. Abbiamo quindi eseguito test su modellino preclinico, su cadavere e poi anche su animale; abbiamo infine studiato il parenchima cerebrale dal punto di vista istologico documentando il danno visibile causato dalla retrazione cerebrale. Questi steps sono stati fondamentali per poi procedere con la fase clinica sui pazienti: i prossimi passi saranno testare il prototipo della spatola sul paziente in sala operatoria e terminare gli ultimi test preclinici della camera. Confidiamo anche di depositare il brevetto per la nuova spatola entro la fine di quest'anno.

1. HUMAN BRAIN, STRUCTURE AND FUNCTIONS

1.1 INTRODUCTION TO THE NERVOUS SYSTEM

The nervous system receives stimuli from both the external and internal environment and analyses them in order to produce adequate and coordinated responses in the various organs. The central nervous system (CNS) is composed of the brain and spinal cord which are connected to the sensory receptors and muscles through long axons that form the peripheral nerves.

The spinal cord is the seat of elementary reflexes, for example that of knee extension and retraction of a limb when subjected to a caloric or stinging stimulus, but also of more complex reflexes.

The brain plays a fundamental role in the acquisition of information, in motor control and in maintaining the body's homeostasis. The brain can be divided into four regions:

1. The **brainstem** contains nerve centres that control, for example, breathing and blood pressure. Through the brain stem, information from the spinal cord reaches the rest of the brain.
2. The **cerebellum** controls posture, balance and coordination of movements and is located at the base of the skull.
3. The **diencephalon**, located above the brain stem in the centre of the skull, is made up of three structures:
 - the **Thalamus** which receives and sorts information deriving from the sense organs;
 - the **Hypothalamus** which controls body temperature, water balance, metabolism and daily biorhythms such as sleep and hunger, is the seat of emotions, the pleasure and addiction centre;
 - the **pituitary gland** a gland of the endocrine system.
4. The **telencephalon** is the most voluminous part of the entire brain.

The brain and spinal cord are covered with three layers of tissue (**meninges**) of different thickness and structure:

- the **dura mater** very thick, adheres to the bony part;
- the **pia mater** very thin and vascularized, adheres to the nervous tissue;
- the **arachnoid** with a network structure, which is located between the other two meninges.

Between the arachnoid and the nervous tissue there is the subarachnoid space, which contains the **cerebrospinal fluid** or "liquor" that fills all the cavities of the central nervous system.

1.2 THE BRAIN

The brain is still considered the most complex organ of our body, capable of controlling many different functions such as memory or language, limb movements and in general the functioning of all organs of the human body.

The development of the human brain starts in the mother's womb. During intrauterine life, the size of the brain increases considerably due to the rapid increase both in the number of specialized cells (neurons) that compose it and in the support structures and connections.

The adult brain is made up of billions of interconnected neurons.

1.3 ANATOMIC STRUCTURE

Anatomically the brain consists of two mirrored cerebral hemispheres which are divided by an interhemispheric sulcus. At the base of the latter, however, the two hemispheres are connected by a network of nerve fibres that make up the corpus callosum:

- The superficial portion of the brain (cerebral cortex) is made up of **grey matter** (containing nerve cells and synaptic connections).
- The deepest portion is made up of **white matter** (nerve fibres).

The surface of the cerebral hemispheres has folds that separate the cerebral convolutions. Deeper introflexions (**sulci or fissures**) allow the hemispheres to be divided into cerebral lobes.

The main portion of the brain is made up of the cerebral hemispheres, in which four lobes (frontal, parietal, temporal and occipital) can be identified.

The hemispheres are connected to the underlying structures through the brain stem. Each of the lobes is specialized for a certain function.

The frontal lobe controls the programming and execution of the movement. The parietal lobe is used for the perception of somatic sensations. While the occipital lobe deals with sight. Finally, the temporal lobe controls hearing, learning and memory.

Many of these functions are performed by both hemispheres, while some by only one. Some areas involved in some higher functions have been identified, such as that of speech which is lateralized to the left in most people.

The pathways from the sensory receptors to the cortex and those from the cortex to the muscles cross. For this reason, the movements of the right side of the body are controlled by the left side of the cortex and vice versa, the left side of the body sends sensory signals to the right hemisphere. However, the two halves of the brain do not work separately, as the left and right cerebral cortex are connected by the corpus callosum.

1.4 NEURONS AND SIGNAL TRANSMISSION

The nervous system is made up of a network of specialized cells known as **neurons** (excitable cells) and supporting cells known as **glia** (non-excitable) cells. The excitability of neurons is determined by the presence of voltage-dependent ion channels in the cell membrane and the nerve impulse is generated precisely by the variation in the membrane potential difference.

If the neuron is stimulated, the membrane potential can increase from approximately - 70 mV to approximately -50 mV (threshold potential). Once this threshold value is reached, many sodium channels open and Na⁺ ions pass from the outside to the inside of the cell. As the concentration of positive charges inside increases, the potential abruptly reverses and reaches a value of +35 mV, which is called action potential. This sequence of events, called membrane depolarization, is immediately followed by the re-establishment of the resting conditions (membrane repolarization).

1.5 DENDRITES AND SYNAPSES

All neurons have the same basic structure. We can distinguish a large cell body, which contains the nucleus and cytoplasm, from which two processes start: dendrites and an axon.

The dendrites are very branched and form synapses, or specialized communication sites, with adjacent neurons and for this reason they can be defined as structures responsible for the entry of information.

The **axon** (or nerve fiber) is a portion of the cell body that extends and ends on other neurons or organs and has the function of transmitting action potentials to the synapse, the area where the axon comes into contact with the dendrites of other neurons.

The synapse is composed of the presynaptic nerve termination separated by a thin area from the postsynaptic component.

Signal transmission in this space occurs by means of neurotransmitters, which are contained in vesicles (synaptic vesicles) thickened at the ends of the axon. The latter contracts synaptic relationships with other neurons.

When the neuron is reached by a stimulus, the synaptic vesicles fuse with the pre-synaptic membrane, pouring their contents into the synaptic space and bind to receptors located on the post-synaptic membrane. The interaction between the neurotransmitter and the receptor triggers a response in the postsynaptic neuron. Specifically, the termination of the axon that conducts the nerve impulse releases the neurotransmitter and the electrical impulse is thus translated into a chemical signal.

The postsynaptic termination that receives the nerve signal has specific receptors on its membrane that are able to bind neurotransmitters. This bond causes electrical changes in the membrane of the postsynaptic neuron. If the threshold value is reached, all of this results in a nerve impulse that travels rapidly and spreads to other neurons. At the cerebral level, real electrical signals are generated that run through the neuronal network. Therefore, brain activity is detectable through the electroencephalogram, capable of highlighting the generation, from the cerebral cortex of different electrical waves depending on the state: alertness, sleep, dream.

2. NEUROSURGICAL OPERATION

2.1 HISTORY OF NEUROSURGERY

Neurosurgery developed late compared to other surgical disciplines and only after the introduction of the principles of asepsis and the discovery of specific cortical areas for certain functions (language, motility, etc.). In fact, the clinical symptom "suggested" to the neurosurgeon the site of the lesion and indicated the limits of the treatment, so as not to damage the functionally important areas. The Italian Durante (1844 -1934) was the first to remove an intracranial meningioma, a benign tumor.

Modern neurosurgery was born with H.W. Cushing (1869-1939) and W. Dandy (1886-1946) in the USA and H. Olivecrona (1891-1980) in Sweden. Cushing invented and described numerous surgical techniques: he identified and classified (with Bailey and Eisenhardt) many of the lesions of the nervous system; he and Bovie developed a device for the control of intraoperative bleeding (haemostasis by electrocoagulation).

Dandy was a pupil of Cushing and he replicated his results sometimes improving them, although often in disagreement with the Master. He invented the first method for studying brain damage: ventriculography. The injection of air into the ventricles made them visible with a common radiological device, detecting the site of the lesion on the basis of their deformation and displacement with respect to the midline.

Olivecrona (1891-1980) distinguished himself in the treatment of vascular malformations, leaving an indelible memory for his technical and organizational skills. Many European and Italian neurosurgeons were trained at his school.

In the 1920s, the Portuguese E. Moniz invented angiography for the radiological visualization of cerebral arteries, opacified with the injection of iodized liquid. It is used for the visualization of the lesions of the vessels (aneurysm) and reveals, for their displacement from the normal position, any lesions.

Functional neurosurgery aims at correcting impaired functions. The pioneer was W. Penfield in Canada, who conceived epilepsy surgery and verified in vivo the functionality of critical areas, such as those of speech or motility. At the same time E. Moniz conceived psychosurgery for the treatment of severe psychiatric disorders. Stereotaxic treatment originated in the USA with E.A. Spiegel and H.T. Wycis and is used for the accurate localization, with mathematical coordinates, of any point in the brain. For example, it allowed to reach deep brain structures involved in motor disorders such as Parkinson's disease.

Modern neurosurgery began in the 1960s with the use of the operating microscope, perfected and widespread by G. Yasargil in Switzerland. The invention in the seventies of computerized axial

tomography (CT) and subsequently of magnetic resonance imaging (MRI), greatly increased the diagnostic and therapeutic possibilities, allowing to see the lesion in its relationships before surgery. Nowadays it is possible to "illuminate" the active brain areas, while computerized systems (neuronavigators) map the surgeon's path as he proceeds.

2.2 CRANIOTOMY

Since the brain is located inside the skull, in order to access it, an intervention that allows its exposure is necessary: the technical term is craniotomy. This is a very standardized surgery; the evolution of surgical instruments and, in particular of drills, has made possible to obtain over the years more precise and safer and above all more aesthetically pleasing results.

Craniotomies can have a different shape and position depending on the brain area that needs to be operated on. The preparation in the operating room for a craniotomy can take a few ten of minutes (to place vascular accesses, catheters, monitoring ...) and the patient must be positioned on the operating table in order to allow the surgeon a correct exposure of the skull.

A craniotomy is performed after the skin and subcutis have been incised with a scalpel. Exposed to the bone, one or more holes are drilled with a drill. The craniotome is then used, an instrument that can be connected to a compressed air or electric power supply. With the craniotome a bone flap (the operculum) is made which completely exposes the dura mater that covers the brain.

At this point the meninges is incised and the brain is exposed. The craniotomy is only the first part of a neurosurgical intervention: once the surgeon has access to the brain, the central phase begins which consists, depending on the different pathology, in the evacuation of a hematoma, in the removal of a tumor or in clipping. of an aneurysm (a sort of clip is placed to close the vascular malformation). In the development of neurosurgery, the introduction of the operating microscope has played a fundamental role, which allows you to enlarge the area in which you operate, in order to be much more precise and accurate.

At the end of the surgery, the part of the skull that has been removed to allow surgical access is repositioned and fixed with some mini-plates made of metal alloys.

In some cases, depending on the position of the area to be operated on and the type of surgery to be performed, the operculum is not replaced: in this case we perform a craniectomy.

3 HISTORY OF BRAIN RETRACTION

3.1 STATE OF ART

Since the earliest medical discover of Hippocrates, the dura mater has been characterized by a strong sense of respect and importance. It wasn't until the nineteenth century that this limit was pushed and brain retraction became an essential part of intracranial surgery.

Brain retractors have recently been devised and developed in order to obtain a better visualization, increase the freedom of manipulation and stability. At the same time, it is essential that these instruments require less and less effort on the part of the surgeon, but above all it is essential to minimize the possible complications of the use of these.

Brain retractors have therefore evolved from simple manual retractors to more complex systems equipped with components capable of stabilizing the retraction.

The first operation we have evidence of is trepanation, which consisted of drilling the bone in order to expose the intracranial contents for both medical and mystical reasons. This procedure dates back to the Mesolithic, before the development of writing and the use of metal tools.

Manual retractors appeared in the assortment of surgical instruments used by the Romans and were presumably kept by assistants to allow the surgeon access to the skull.

Hippocrates was the first to mention the use description and procedure of trepanation in his treatise *On Wounds of the Head*. His toolset included a drill, a serrated drill, a chisel, and a probe. The probe that served as a retractor and protection for the dura mater during craniotomy, as it was placed in the drilling hole to determine the depth and mobility of the underlying bone. Despite some exceptions, cranial surgery from the time of Hippocrates up to the eighteenth century focused mainly on head trauma, with particular attention to the dura mater and brain parenchyma, and the only necessary retraction was that of the extra axial soft tissue.

In his book on skull fractures, Jacopo Berengario da Carpi (1460-1530 AD) illustrates a retractor used to drill during the sixteenth century. However, many surgical instruments of the sixteenth and seventeenth centuries were decorative, large and shabby.

Significant innovations occurred in the field of brain surgery during the second half of the nineteenth century. Advances in cerebral localization, anaesthesia, control of intracranial pressure, antisepsis and aseptic techniques thanks to which it was possible to significantly reduce the morbidity and mortality associated with neurosurgery, allowing neurosurgeons to take more energetic actions in the management of cranial pathologies.

As intracranial surgery became less risky and neurosurgeons more comfortable working deeper into the brain, a growing need for brain retractors developed. Initially, the cerebral retraction took place

thanks to manual retractors, which required an assistant to hold them. However, in addition to the assistant's hand obscuring vision and limiting light, his mistakes or his fatigue could cause the retractors to slide out of the desired position, causing excessive retraction or damage to the brain parenchyma and other structures.

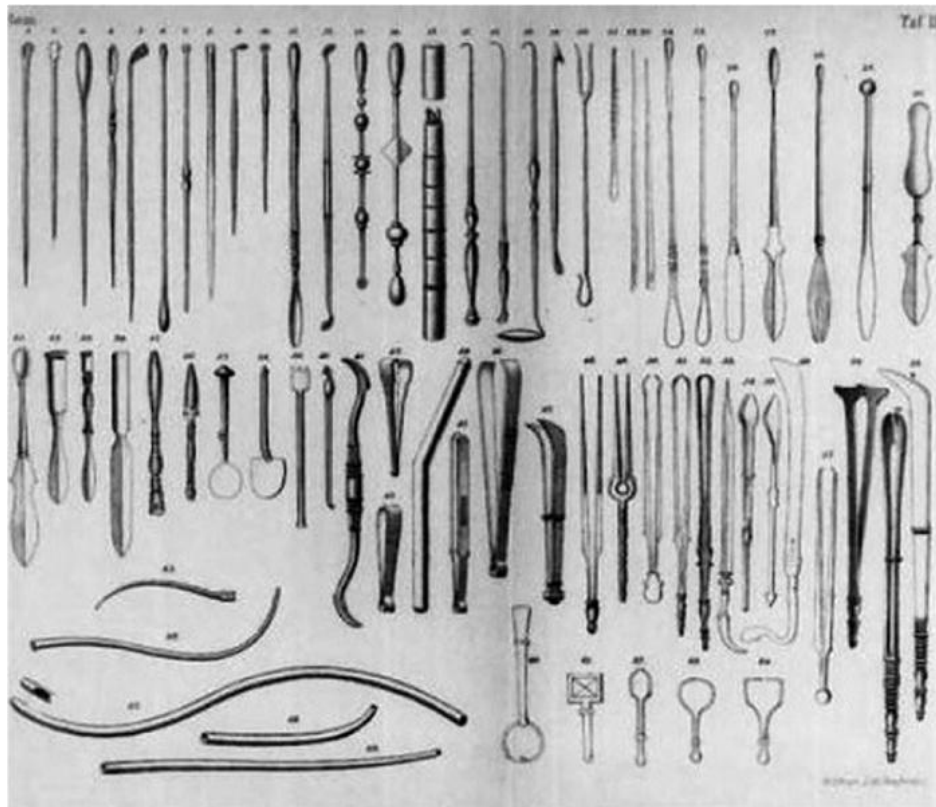
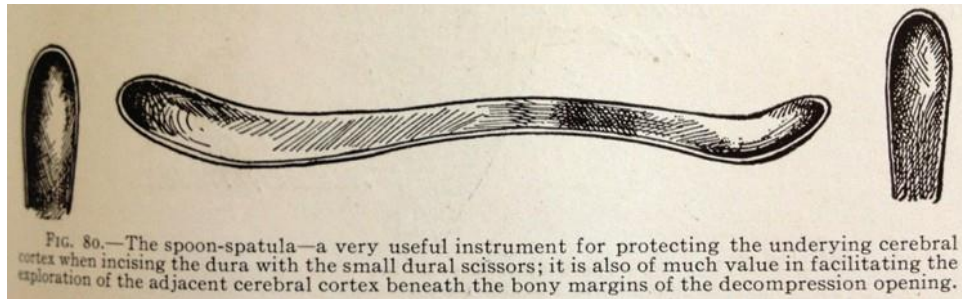


Illustration of the variety of sizes and shapes of manual retractors that are part of the surgical tools used by the Romans. (Illustration by Ernst Julius Gurlt, 1898)

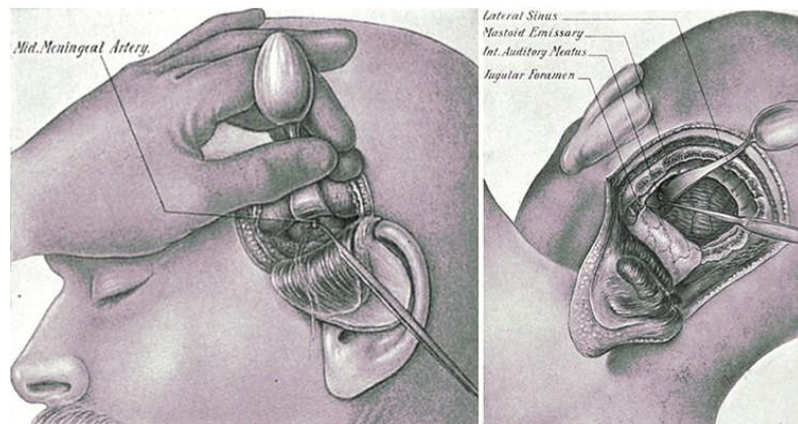
Manual cerebral retraction

In 1879 William Macewen (1848-1924) successfully resected the first brain tumour, a frontal meningioma. Sir Rickman Godlee (1849-1925) performed the first intracranial brain tumour operation for a glioma in 1884: he used a narrow spatula to separate the tumour from the brain parenchyma. The patient survived the surgery, but died of dehiscence and wound infection a month later. William Williams Keen (1837-1932), the first US neurosurgeon, used spoon and spoon handles in his 1882 intracranial operations. In 1890 Alec Fraser, in his operative text 'A Guide to Operations on the Brain', gave instructions regarding the placement of manual retractors. In 1901 Lothar Heidenhain (1860-1940) described the use of thin spatulas of various sizes to delineate tumours under direct vision. Later, in addition to using spoon handles for brain retraction, Charles Frazier (1870-1936) developed an elevator that could be used in operations at the base of the brain. This retractor

was unique in shape and thickness: the angle of the handle was located so that the hand holding the retractor did not obscure the surgeon's field of operation and the blade was thick enough to flex evenly under pressure. In some situations, Frazier used both his elevator and spoon retractor to facilitate resection of the tumour. Sir Victor Alexander Haden Horsley (1857-1916), known as the first surgeon able to successfully remove a spinal cord tumour, performed many intracranial surgeries in which he used brain retraction in 1887, in addition leaving numerous writings to the regard.



Spoon spatula by Dr. William Sharpe (1882-1960), probably very similar to that used by William Williams Keen. ('Neurosurgery: Principles, Diagnosis, and Treatment', J.B. Lippincott, 1928)



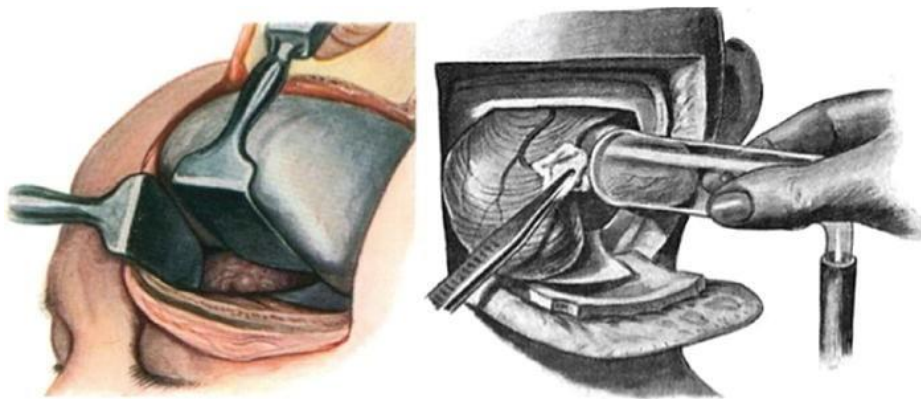
*Hand-held spoon retractor, illustration from 1909
('Surgery: Its Principles and Practice, Vol. 5)*

In 1909, William Harvey Cushing (1869-1939), the father of American neurosurgery, used a rounded-edged spoon-shaped retractor causing less damage to cortical vessels than flat, sharp-edged retractors. Cushing and Horsley have therefore both introduced manual retractors designed as rectangular belts that can be molded as needed. Cushing describes the use of manual retraction in the removal of olfactory sulcus meningiomas, commenting on how the lower surface of the frontal lobe must be elevated and displaced to expose enough tumour.

In 1913 Thierry de Martel (1875–1940) one of the founders of neurosurgery in France, introduced a malleable retractor which he attached to the margin of the cranial defect.

Around this same time, Fedor Krause (1857–1937), the father of German neurosurgery, was employing, in addition to manual rounded-edge retractors, a suction-retraction technique to help stabilize, expose and remove gliomas.

In 1926 Hans Brun (1874–1947) recommended a cautious injection of saline around the lesion to help separate the tumour from normal brain parenchyma.



Left: Krause retraction of the frontal lobe with a manual retractor to approach a meningioma located in the skull base. Right: Krause uses a new method that involved vacuum aspiration of the tumour mass to facilitate non-traumatic dissection, especially within the posterior fossa. (Illustrations from 'Surgery of the Brain and Spinal Cord')

While Temple Fay (1895-1963) is often credited with developing the first retractor with illumination in 1927 to facilitate exposure during the operation. However, there is evidence that his mentor, Charles Frazier, used a device that had previously been lit, as described in the 1921 Annals of Surgery. Furthermore, in the 1922 text 'Surgery Its Principles and Practice', Frazier describes the use of his retractor with illumination in trigeminal nerve surgeries.

There is also evidence that in 1920 Alfred Washington Adson (1887-1951) used a retractor equipped with illumination for the elevation of the temporal lobe during surgery along the trigeminal ganglion.

Self-locking retractors

The first self-locking retractors were screw-type: in 1895 such mechanisms were used to open retractors and Broz's wound dilator was a famous example. These retractors were complicated to handle - they required two hands to place them, they were difficult to clean and the screw mechanism

was often inaccessible once in place. To overcome these shortcomings, Franz Weitlaner, (1872-1944), an Italian physician working in Ottenthal, Austria, developed the 'Weitlaner' retractor in 1905.

Regarding the specific self-locking retractors for cranial neurosurgery, there are four categories:

- mounted on the skull, i.e. directly attached to the skull or indirectly fixed with a special clamp;
- mounted on soft tissues, therefore secured by tension in the muscles and soft tissues;
- mounted to the operating table;
- mounted on the headrest, which are attached to the skull clamp.

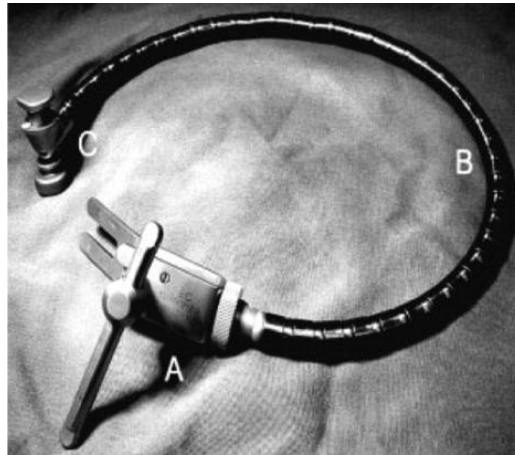
Skull-mounted retractors

In 1930 Thierry de Martel developed the first skull-mounted retractor, which consisted of a cylindrical metal post inserted on one end of the skull and a rectangular retractor on the other. However, this instrument had limitations: each retraction blade required its own hole and the varying thickness and strength of the skull did not allow for pin placement in all craniotomy positions. Norman (1897–1973) often described as the "engineering surgeon", developed a skull-mounted retractor that he described as "the nice little machine we use to keep the brain out of the way when dealing with tumours. difficult to access. "

The Gillingham retractor solved some problems by attaching multiple retractors to a rod.

In 1937, Wallace Hamby (1903–1999) developed a clamp that connected the retractors to the rim of the craniotomy to obviate the need to drill additional holes in the skull. However, this too depended on the thickness of the skull and was not usable in all positions.

Subsequently, Theodore Kurze's first neurosurgical use of the operating microscope in 1957 and the development of microsurgery in the following decade led to the creation of numerous new microsurgical instruments and the improvement of existing instruments, including brain retractors. The retractor blades remained fairly similar, but the main changes occurred in the fixation of the blade: no movement of the retractor blade or head was acceptable anymore during surgery. To this end the Malis and Heifetz retractors, which were developed in the late 1970s, allowed multiple blades to attach to one attachment point: in a hole or on the edge of the skull. Additionally, these retractors offered surgeons more customized options: they included various shaft lengths and multiple blade attachment points along each shaft. Mahmut Gazi Yaşargil (1925–), a Turkish neurosurgeon, in 1968 developed another flexible self-locking retractor known as the Leyla retractor, initially attached to the rim of the craniotomy. However, difficulties in obtaining adequate clamping of the arm can cause the retractor to move during use. Additionally, a long arm interferes with the surgeon's hands and causes damage to the dura and soft tissue around the clamp. As a result, the Leyla retractor attachment was moved to the operating table rather than to the rim of the craniotomy.



Leyla retractor, self-locking and skull mounted with flexible arm and spatula attached to its end. (From "Neurol Res", Dujovny, 2010)

Retractors mounted on soft tissue

Soft tissue-mounted retractors, such as the Weitlaner, were among the first retractors in neurosurgery to provide access to the skull while keeping these tissues out of the surgical field. In 1961 the House-Urban retractor was developed described as a modified Weitlaner that provided extradural elevation of the temporal lobe. Later Peter J. Jannetta (1932) modified the Weitlaner soft tissue retractor in 1973 by attaching two posts to each arm of the retractor, allowing the attachment of rods and blades to perform cerebellar retraction. He eliminated some of the inherent instability of the soft-tissue-mounted retractor by attaching it to surgical drapes.

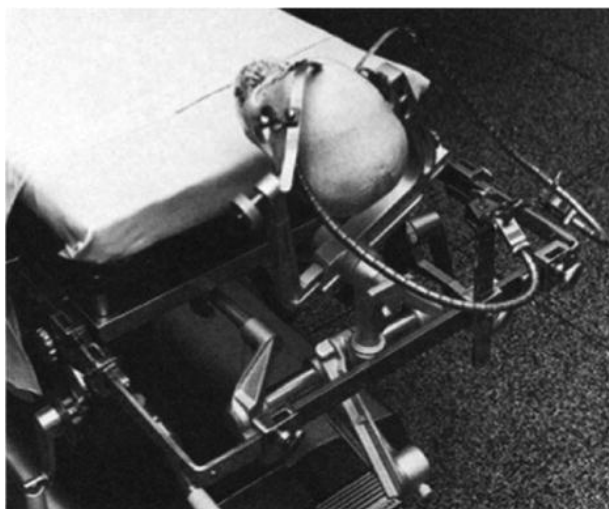
Instead in the early 1980s the Apfelbaum retractor was developed, which contained a flexible shaft and rounded retraction blades to minimize excessive cerebellar compression.

Later the cerebellar retractors Miskimon, Cloward and Enker were developed: these are soft tissue retractors that use malleable retraction blades. Although useful and pragmatically developed at the time, a common limitation presented by soft tissue retractors is that the support system for retraction is very close to the operative site, so the joints provided by the retractor arms and blades are insufficient to provide retraction from all angles.

Table mounted retractors

This type of retractor helped to solve the above limitations by fixing the base of the retractor to the operating table. Notably, in 1974, Yaşargil and Fox attached the Leyla retractor to the support bar of the Aesculap retractor. Later in 1976 Jose Kanshepolksy developed a U-shaped frame that served as

an attachment point for the base of the retractors. However, these systems also have disadvantages: the possibility of independent movements of the head or of the retractor arm cause uncontrolled movements at the brain-retractor interface and the amplification of any movement in the direction of the retractor arms.



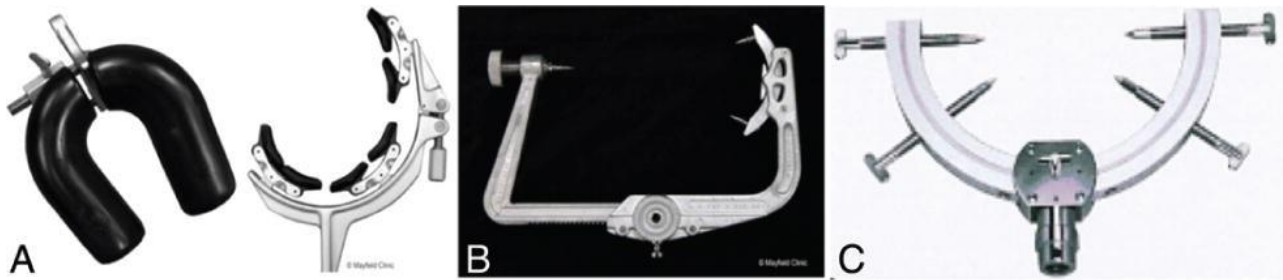
In this photograph, a double-arm Yaşargil-Leyla brain retractor was attached to the extracranial support. This equipment is positioned for a right-sided craniotomy. Technical Note J Neurosurg 46: 835–836, 1977.

Retractors mounted to the headrest

In 1967, Frank Mayfield (1908–1991) and George Kees (1925–2010) developed the Mayfield “Horseshoe” and “General Purpose” head restraints to better support and stabilize the head during operations. With the advent of microsurgery and subsequent minor craniotomies with improved head stabilization, Mayfield and Kees developed the Mayfield Three-Pronged Skull Forceps in 1973. Later Kenichiro Sugita (1932–1994), a Japanese neurosurgeon, also developed a four-pin fixation head support in 1978. Skull clamps, such as “the Mayfield” and “the Sugita” are securely attached to the skull and then to the operating table, theoretically eliminating any possibility of head movement. Therefore, the greater distance from the craniotomy site and their rigid attachment to the table made these three- or four-point headrests ideal for supporting the base of self-locking retractors. Mark S. Greenberg, Kenichiro Sugita, Takanori Fukushima and Keiji Sano have all developed self-locking retraction systems that attach to the skull clamps. Greenberg’s retractor and hand rest system was developed in 1975 and consists of primary clamps, secondary clamps, flexible rod holders, retractor blades and palm rests for stabilization.

Then in 1977, the Sugita system was devised, consisting of a head support with a frame attached to it to hold flexible self-locking retractors, hand rests, stands for microsurgical instruments, a plate for cotton discs and spring retractors for flaps of skin.

In 1981, Richard Budde and Jim Day developed the "Budde Halo Brain Retractor System". This system was designed to be attached to the Mayfield Skull Clamp.



The most commonly used neurosurgical tools around the world, which help stabilize the patient's head during surgery. A: The Mayfield horseshoe headrest (left) and the general purpose headrest (right). Used with permission from the Mayfield Clinic. B: The Mayfield Three Point Head Mount. Used with permission from the Mayfield Clinic. C: The Sugita Four Point Head Mount, designed in 1978.

Other retraction techniques

Today, in the 21st century, surgeons and scholars are still looking for ways to improve brain visualization during surgery, ensuring that the brain parenchyma remains unharmed.

In 2000, special spoon retractors were developed, useful for retracting and removing soft tissue masses. They are designed with an eggshell-like concave shape to allow for upward retraction. This allows for the creation of sufficient space to dissect the soft masses from the surrounding tissues in the operative field.

In 2006 Serarslan and others designed an air-filled, cotton-filled microballoon device for use between metal retractors and the surface of the brain to minimize operational damage to the brain parenchyma. Their materials have been noted to help minimize tissue damage and aid in the separation of sulcus and cistern walls during surgery. Giannantonio Spena and Pietro Versari reported the use of balloon tips of Fogarty catheters for mild brain retraction in cases involving aneurysms of the anterior circulation, as well as for brain tumours of the base and midline of the skull. Described as a less traumatic and more dynamic method to aid in vision during the operation, they suggest that their method may act as an alternative to the use of self-locking retractors. In addition, tubular retractors have been used in neurosurgery to access deep brain lesions and these decrease the effects of retraction on the parenchyma.

Finally, the ViewSite Tubular Retraction System has proven its effectiveness in retraction for both adults and children for the removal of tumours in deep areas.



ViewSite Tubular Retraction System. Tubular retractors disperse the retraction force over a larger surface area than standard retractors, helping to minimize parenchymal damage.

With the development of neurosurgery, the need to retract the brain in order to reach deeply located lesions has become increasingly evident.

The retraction must be carried out with appropriate tools that allow to obtain not only the visualization of the site but also the space necessary for the surgeon to access and move the instruments.

Currently, the most common tools for cerebral retraction are spatulas: these tools are generally flat and can have different geometry and dimensions. They are manually moved by the surgeon and, being made of metal material, they can be bent at will in order to obtain the most suitable curvature for the retraction site.

Very complex neurosurgical operations can last several hours and therefore manually managing the retraction can be difficult and unsafe due to human errors connected to the fatigue and effort required. To overcome this problem, various solutions have been developed for the mechanical support of retractors. The spatulas can thus be fixed to the operating table, to the headrest or even to the skull itself using special clamps applicable to the edge of the bone.

The last frontier of cerebral retraction are tubular retractors. These tools differ in shape and geometry from the spatulas being in fact made in tubular form. Their section, circular or ovoid, is not constant but decreases in axial development. In this way, the narrower section is inserted into the brain more easily.

They are generally used with a shutter: component with a geometry similar to the retractor that is inserted inside this in order to make insertion easier and less traumatic. The shutter ends in fact with a tapered shape suitable for moving the fabric.

The real innovation of this technology is the use of transparent plastic material that allows you to monitor the retracted fabric, moment by moment, in order to prevent possible injuries.

This device was born and is still used in operations for the removal of cerebral hematomas, a pathology that requires easier retraction given the radial development of the hematomas: this facilitation is not present in tumour removal operations where the lesion is deep and covered with healthy tissue that needs to be retracted.

3.2 BRAIN RETRACTION INJURIES

Thanks to the advent of ever new technologies, even very complex interventions are now possible, especially in the oncology field. The refinement of microsurgical techniques has made it possible to carry out increasingly complex approaches, which can allow the removal of tumours located in eloquent areas of the brain. To reach these lesions, often located in very deep areas of the brain, however, it is necessary to create a suitable space for the passage of surgical instruments in order to reach the specific target.

The result is the need to move portions of the brain parenchyma, even sometimes in contact with the bones of the skull, in order to obtain sufficient space to operate; therefore, from this necessity tools for cerebral retraction were born.

Retractors are often essential for the success of the surgery but one of the difficulties in the neurosurgical field is precisely maintaining a consistent cerebral retraction.

In some surgical situations, the operating field is so restricted that the assistant's hand, aimed at keeping the retractor in position, tends to further reduce the space required to access. It may therefore be useful to use microscopes in order to expand visibility.

The greatest limitation to the use of brain retractors is their high possibility of causing damage to the parenchyma. This is especially evident when it comes to interventions lasting many hours which therefore require a long-lasting cerebral spatulation.

Possible damage from cerebral retraction can include bruises, hematomas and haemorrhages. The first two are caused by direct trauma on the cortex which then reacts by swelling; haemorrhages can instead be caused by direct trauma on the cortex and subcortical layer, or by indirect trauma on the same vessels that rupture causing blood to leak into the surrounding brain.

These lesions may be visible intraoperatively, but it has been seen that often the micro-lesions, not macroscopically visible but also a possible source of neurological deficit, are visualized with postoperative radiological investigations such as CT and MRI of the brain.

These damages are particularly severe in children. In fact, in children the intracranial space is smaller in size and, therefore, access to the disease can be very difficult. This results in a necessary need to create space for the surgical approach and, therefore, the need to retract the brain.

The exact paediatric blood pressure threshold beyond which there is damage to the brain parenchyma is not known, however there are several cases reported in the literature of post-operative deficit due to cerebral retraction.

Cerebral retraction involves pressure on the surface of the brain which is consequently discharged onto the underlying tissue, the subcortical parenchyma or white matter. This action can also cause a partial or total closure of blood vessels and therefore also compromise the supply of oxygen to the cells of the brain.

The severity of the damage certainly depends on many factors that act in a different but summation way: the distribution of the retraction pressure, the shape, the geometry of the retractor, the properties of the type of tissue retracted and the vascular pressure during retraction.

In addition to the aforementioned primary lesions such as contusions, hematomas and haemorrhages, there may then be the so-called secondary lesions, connected to the physiology of the brain, which are aggravated by systemic conditions such as hypotension, hypoxemia, hypercapnia.

From the data of the literature it has been seen that, if the mean arterial pressure falls below 70 mmHg with respect to the retraction pressure, the brain is damaged; on the other hand, if this difference remains above 200 mmHg, the brain is completely preserved.

Some studies have also revealed another interesting fact relating to the "regional blood flow" (rCBF): this must be kept greater than 10-13 ml per 100 g per minute to avoid damage.

To protect the brain during a long operation, it is necessary to monitor that the pressure is kept within a certain level for the entire duration of the operation.

The greatest obstacle in developing safe retraction lies precisely in the lack of instruments capable of measuring the pressure exerted on the retracted tissue.

In modern neurosurgery, retractors have evolved into more complex systems that include articulated supports and increasingly performing geometries.

Brain retraction, despite the developments achieved, remains a non-negligible threat to brain tissue since there is a lack of technology capable of detecting the pressure that is being applied.

3.3 INTERMITTENT RETRACTION

In order to investigate the nature of the borderline conditions of brain damage due to retraction, it is particularly interesting to report the results of the aforementioned studies on intermittent retraction. This particular practice is compared to normal retraction and described as less damaging to the retracted tissue. This result helps to have a broader perspective and introduces a new variable in the damage process, which is time.

Several studies have been conducted with pigs to evaluate the benefits of intermittent retraction versus continuous retraction. In the article by J. Rosenorn and N. H. Diemer et al. Cerebral retraction pressure (PRC) was monitored and correlated with regional cerebral blood flow (rCBF) in rats. It has been shown that for PRC values of 30-40 mmHg maintained for 15 or more minutes they cause severe drops in rCBF and consequent brain damage.

With the same experiment model, an intermittent PRC of 40 mmHg was applied, maintained for 5 and 7 minutes with one-minute intervals, without applying pressure for a total test time of 29 and 31 minutes without producing retraction lesions. Only for continuous pressure maintenance over 10 minutes did we start to observe lesions to the retracted tissue.

As regards the decreases in rCBF values, sufficient recirculation (70-90ml / 100g / min) was achieved in one minute and no change in rCBF was detected in the 10 minutes following the interruption of pressure.

Judging from these results, intermittent PRC is preferred over continuous PRC and the PRC maintenance cut-off time of 40 mmHg is approximately 7 minutes. For these PRC ranges the rCBF is quickly restored, so only good release times are needed to avoid critical flow drops.

If the PRC values during an intracranial operation are higher than 30 mmHg and maintained for longer than 8-10 minutes, there is a non-negligible risk of injury from cerebral ischemia. These conditions are aggravated in the case of induced hypotension, a procedure commonly used in intracranial vascular surgery, especially in the case of aneurysms.

It is therefore essential to understand the effects of pressure on the blood flow, to understand what the critical values are and how quickly it is possible to return to a safe condition.

The results on animals may have some deviation from the description of the human brain: the anatomy of the blood vessels and the brain itself is different, in particular the human brain parenchyma has a more convoluted surface that could better protect the regional arteries.

In some human cases the reduction of rCBF was less accentuated thanks to the collateral blood circulation and it was possible to maintain an elevated PRC for longer times.

In practice, all these conditions cannot be monitored on the individual patient and it is necessary to refer to the 7-minute threshold time for high PRC values: this is a general guideline in intracranial surgery.

In another study a similar comparison was made between continuous and intermittent brain retraction in dogs. Here the cerebral retraction was imprinted in control of force expressed in grams. Continuous retraction was applied for 60 minutes with constant forces ranging from 20 to 70 g.

For intermittent retraction the loading period is 10 minutes followed by 5 minutes of release, all repeated six times. The same retraction forces were applied for both tests.

Electrocorticography (ECoG, recording of the action potentials of the cerebral cortex and their variations induced by the various experimental situations) was used to monitor brain functions.

The morphological study showed an aggravation of the damage in the continuous retraction. The samples were treated with a particular dye that highlights the damaged tissue (Blue Evans, a dye that tends to bind to albumin, the tissue is permeable to this protein only in pathological conditions such as haemorrhages which are then highlighted by the dye). The samples show an increasing percentage of colouring (spots) as the force applied increases.

At 20g, 25% of the samples have spots, without bleeding.

At 30g 70% of the samples have spots. 50% have point haemorrhages.

At 40g, 100% of the samples show bleeding and bleeding.

At 50g haemorrhages and bruises are always present and extend to the surrounding white matter, in some cases to the cortical grey matter.

At 60g, the bruised area is so large that in one third of cases the arachnoid membrane is torn.

At 70g the membrane is always torn.

Regarding intermittent retraction:

At 20 and 30g no changes are observed.

At 40g, 33% of the samples show spots (again change the term as before or specify it in the context of the radiological examination or what they did) without bleeding.

At 50g, 100% of the samples had spots, 66% had bleeding but no contusion was found.

At 60g, 100% of the samples have bruises.

At 70g the results are comparable to those of a continuous retraction with an equal retraction force.

On average, an additional 20g of force was required to produce the same degree of injury with an intermittent retraction as a continuous one.

The study of the electrocorticogram has also highlighted how a continuous retraction is more burdensome than a discontinuous one.

The continuous retraction at 30 and 40 g resulted in an average decrease in power in the ECoG of 50% with a rapid recovery after releasing the retraction.

With a continuous retraction at 50 and 60 g, an (average) drop in power in the ECoG was observed equal to 90%. This pressure drop is not recovered quickly: in some of the specimens complete recovery was not achieved even in the three hours following the end of which the guinea pigs were sacrificed for subsequent analyses.

With intermittent retraction at 40 and 50 g the decrease in power reaches 70% but is immediately recovered during the release intervals. This rapid recovery allows the intermittent retraction at 40 and 50g to be compared to the continuous retraction at 30 and 40g.

Intermittent retraction is therefore a safer and less burdensome procedure for the retracted tissue. As for the threshold force and pressure values obtained in the various studies, these are very dispersed due to the different test and pressure measurement methods.

4. LIMITS OF ACTUALLY TECHNOLOGY SOLUTIONS

Brain retraction, despite continuous developments, remains a necessary procedure for the success of the surgery, although it is not without risks for the patient. Several studies report, in fact, a high rate of complications due to the violation of the brain given by the retraction which, for operations at the base of the skull (skull base surgery), reach 10% and 5% in the case of intracranial aneurysms.

Radiologically, it is found that ischemia caused by the retraction blade occurs in approximately 22% of patients in postoperative CT (computed tomography) scans, while oedema in the Sylvian fissure region can occur in 47% of patients operated on for aneurysms of the middle cerebral artery. According to MRI scans (magnetic resonance imaging), permanent lesions caused by retraction were observed in 36% of the cases of surgical interventions on aneurysms of the anterior circulation.

The technologies currently available lack some limitations found in the experience of surgeons and also reported in the literature.

The geometry of the retractor must be able to adapt to the retracted tissue, in order to avoid stress concentrations and deformations on the tissue which is therefore subjected to higher pressures.

As reported in several studies the retractors with flat shape spatulate the tissue with focused pressures and, therefore, more dangerous.

The inability of the retractor to follow the tissue, during spatulation, leads to the development of an acute pressure gradient, at the edge of the spatula, with the consequent risk of injuring the brain parenchyma.

Otherwise, retractors with curved (cylindrical) profile can apply pressure on a larger surface and thus discharge the forces radially, thus obtaining the retraction of the tissue with homogeneous and reduced pressure values.

A curved geometry allows the retractor to be rotated and to change the angle of approach without applying additional pressure, thus increasing the manoeuvrability of the instrument.

The transparency of the retractor is strictly connected to the possibility of constantly monitoring the conditions of the underlying parenchyma, displaying possible damage such as bruises or haemorrhages and being able, therefore, to act promptly to resolve them.

The possibility of using a transparent retractor has been described as an advantage by surgeons as it allows to constantly monitor the retracted brain and also better visualize the dimensional limits of the lesion without having to move the instrument further.

Spatulas made of metal do not allow you to view the site of the retraction and, therefore, any damage connected to it. Transparency, combined with a specific robustness of the device, is particularly advantageous during its insertion: it can in fact be carried out by displaying the trajectory of advancement.

The Tubular retractors deserve a special mention, which as previously described, have proposed themselves as the last frontier of cerebral retraction, enjoying both a geometry suitable for retraction and an appreciated transparency.

This type of device is currently used for the removal of hematomas that do not have the same complexities as the operations for the removal of the tumour. In fact, the tumour can develop in depth leaving intact the overlying tissue which becomes an obstacle to reaching the site of the operation, the hematomas instead have a radial development and do not reach great depths, allowing less problems in the retraction phase and more ease in the operative gesture: the hematoma is in fact easily aspirated having a different consistency than that of the tumour parenchyma.

To date, tubular retractors cannot replace blade retractors which still remain the most used instrument in neurosurgical operations.

In fact, several surgeons find the corridor obtained from the tubular retraction too narrow to be able to operate easily. These tools, although available in various sizes, are inherently rigid tools; their insertion does not provide for a control on the retraction and it is not possible, for example, to control the speed with which the tissue is moved.

Furthermore, in another study, the extension of the operating field provided was found to be limiting: the opening of the retractor on the lesion is even narrower than the canal due to the tapered shape.

The same authors also state that the retraction obtained with the spatulas could be less invasive than the tubular retraction, because the latter requires continuous repositioning, especially in the case of voluminous and deep lesions. Such repositioning manoeuvres could be dangerous given the rigidity of the instrument and the impossibility of adapting its shape to the operating site.

Another limit of this technology is the rigidity of the retractor itself which in fact decreases the manoeuvrability and the stability: just consider, for example, that as you proceed with tumour resection, the retractor loses stability due to the new space created.

Finally, the instruments currently used in surgical interventions do not provide a confirmation of the pressure or force values applied during parenchymal retraction. Therefore, the surgeons do not know, in real time, the effects of the retraction on the retracted tissue and this implies a serious limit to the achievement of the surgical goal. This becomes evident in very long operation where there is the difficulty of manually maintaining a certain position (and a certain strength) stable for the entire duration of a neurosurgical operation, which can reach up to 6-8 hours.

Moreover, in the literature reliable critical values of pressure threshold have been hypothesized beyond which damage to the brain can occur.

To date, there is still no brain retraction system that can be considered safe with certainty.

5. MECHANICAL BEHAVIOUR OF BRAIN

5.1 HOMOGENEOUS AND ISOTROPIC LINEAR ELASTIC BOND

It is of great importance to understand the mechanical response of the brain tissue in order to be able to create models and simulations that allow to predict the effects of a load applied to the brain parenchyma and any damage.

This type of constitutive equation is among the simplest and is based on several important assumptions about the material being considered:

- Elastic, with reversible behaviour, i.e. if the body is loaded, deformed and subsequently unloaded, the sample will return exactly to the starting conditions following the same deformation path;
- Linear, stresses and strains are linked through a linear relationship;
- Isotropic, the response of the material is independent of the direction of stress;
- Homogeneous, the material properties are constant at every point.

The equations that describe this model are:

$$\begin{aligned}\varepsilon_{xx} &= \frac{\sigma_{xx}}{E} - \frac{\nu}{E}(\sigma_{yy} + \sigma_{zz}) \\ \varepsilon_{yy} &= \frac{\sigma_{yy}}{E} - \frac{\nu}{E}(\sigma_{xx} + \sigma_{zz}) \\ \varepsilon_{zz} &= \frac{\sigma_{zz}}{E} - \frac{\nu}{E}(\sigma_{xx} + \sigma_{yy}) \\ \varepsilon_{xy} &= \frac{\tau_{xy}}{G} \\ \varepsilon_{xz} &= \frac{\tau_{xz}}{G} \\ \varepsilon_{yz} &= \frac{\tau_{yz}}{G}\end{aligned}$$

Where E is the elastic modulus and is the elastic constant binds the stresses in one direction to the deformations in the same direction. G is the shear modulus of elasticity and similarly links the tangential stresses to the tangential strains. Finally, ν is the Poisson's ratio and links the strains in one direction to the stresses in the two orthogonal directions. It is important to remember that only two of these elastic constants are linearly independent in fact:

$$G = \frac{E}{2(1 + \nu)}$$

5.2 VISCOELASTICITY

With viscoelastic materials we refer to those materials that under the action of a force show an intermediate behaviour between that of elastic solids and that of fluids: their response to stress is partly elastic and partly viscous.

5.3 DYNAMIC MECHANICAL BRAIN BEHAVIOUR

Since the early 1960s, studies have been conducted to arrive at a description of the mechanical properties of the brain.

Finding a valid constitutive equation for the brain would then serve to be able to implement a finite element model. A valuable tool for investigating the nature of the stresses and deformations associated with damage processes.

The literature presents a large number of very heterogeneous studies. In fact, experiments have been conducted on both animals and humans. Furthermore, the tests may have been performed in vitro or in vivo as well as presenting different testing methods and protocols.

The experimental results present in the literature are therefore dispersed and not easy to interpret.

We recently published a study about brain tissue dynamic behaviour pointing out new insight into the material nonlinear viscoelasticity.

Shear dynamic response curves are obtained in different working conditions in terms of strain sweep and superimposed static compression offsets (SCO) applied in orthogonal direction to the shear.

The strain sweep mode is used to study the storage and loss moduli dependence on the amplitude of the applied strain. It is found that the material exhibits linear viscoelastic behaviour up to about 0.1% strain amplitude. Above this critical threshold, the storage modulus G' decreases rapidly with increasing dynamic strain amplitude and this effect is gradually intensified as the SCO are increased. In addition, it is observed that the loss factor (G''/G') increases by increasing the SCO applied to the specimens. The dynamic strain amplitude results of the storage modulus reveal that the elastic component of the brain tissue's stiffness (G') evaluated at low strain strongly increases with increasing static superimposed compression strain while the loss factor in the same strain range appears to be SCO independent.

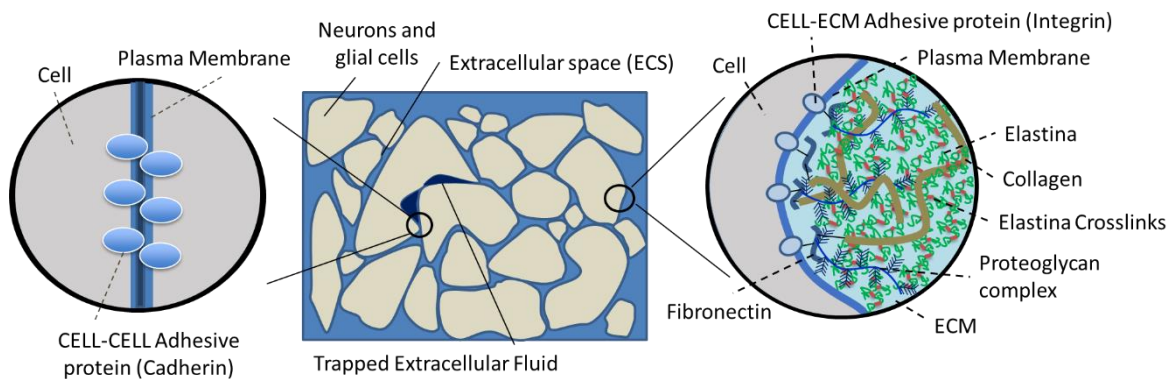
Finally, dynamic stiffness recovery after a large strain deformation is considered. The reduction in low amplitude dynamic modulus and subsequent recovery kinetics due to a perturbation is found to be independent of the level of the SCO.

The same assessments were carried out on 5 consecutive strain sweep cycle loading. It has been noticed that at the last cycle, the dissipation peak is reduced, and the non-linearity of the curve begins

earlier. This could be explained by the effects of cerebral oedema on cells and their surrounding environment.

Brain parenchyma not homogeneous, it is a biphasic material:

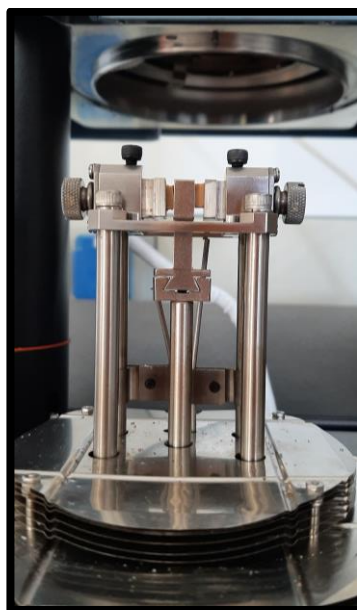
- Extracellular matrix (ECM), neurons, glial cells, and capillaries: Solid Viscoelastic component;
- Free-flowing fluid (FFF) within the network: Liquid Viscous component.



Brain parenchyma composition

Brain sample deformed in shear with superimposed static compression

We performed solid test specimens with shear mode at various levels of strain amplitude in superimposed static compression offset at a temperature of 25°C, frequency of 1 Hz. Our objective is to study elastic and viscous stresses related to material properties through the ratio of stress to strain: the modulus.



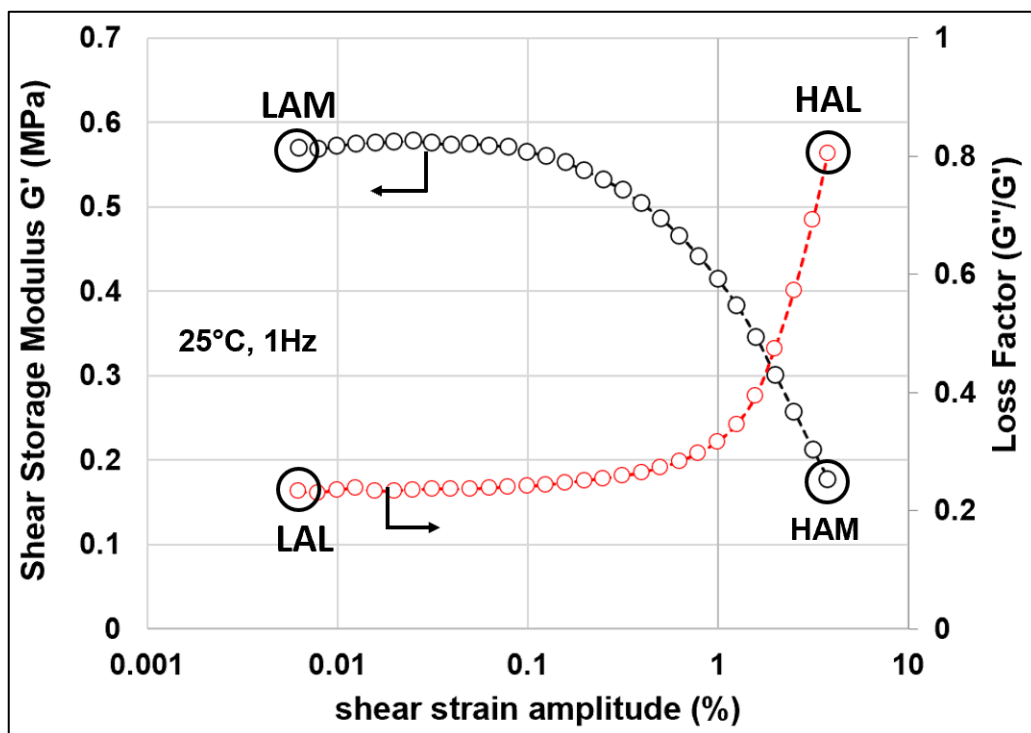
Laboratory tests of static compression

Nonlinear viscoelasticity

Storage modulus G' is the energy stored in the elastic structure of the specimens and it is independent of shear strain amplitude below a critical strain amplitude (of about 0.1%), beyond which it decreases rapidly.

This strain dependence of complex dynamic modulus, qualitatively similar to that observed in filled elastomers, represented the "Payne effect".

Ratio of the elastic stress to strain: **elastic (or storage) Modulus G'**



Ratio of the viscous stress to strain: **viscous (or loss) Modulus G''**

Microstructural reorganization

There is a microstructural reorganization of brain:

- reduction of cell-cell and cell-ECM interaction through the main adhesion proteins (cadherin and integrin respectively);
- ECM network subversion and disentanglements (collagen, elastin);
- release of the hydrostatic pressure exerted on FFF with consequently flow in areas of lower pressure

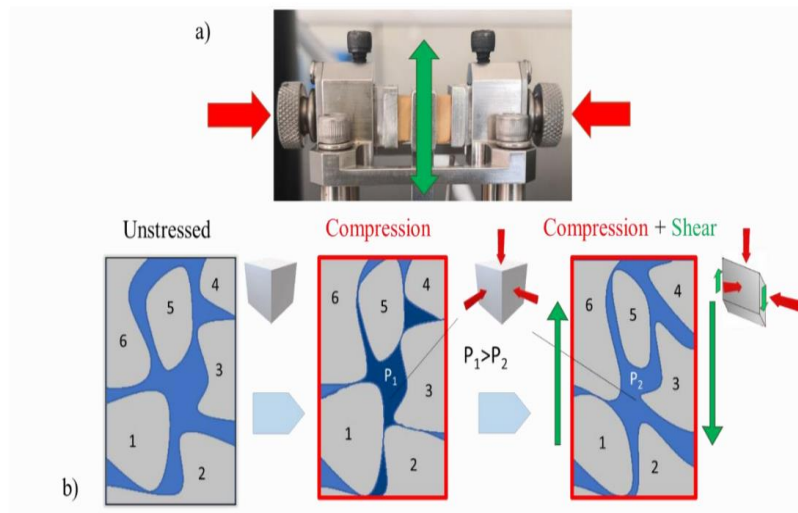
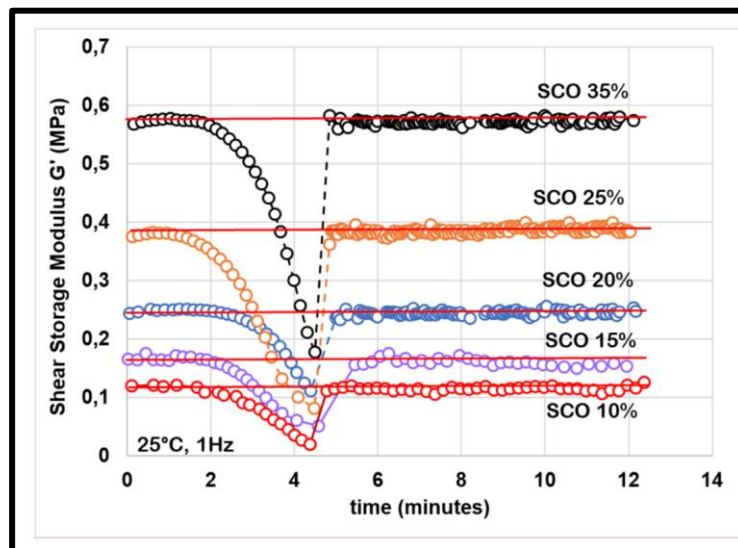


Fig. 6 a) Shear assembly configuration b) Schematic cellular and extracellular fluid rearrangement during the dynamic shear test. The superimposed compression preload increases the cell-cell surface interactions and the FFF; the shear at high amplitude allows the extracellular fluid to flow in another region.

Dynamic stiffness recovery

We noticed that there is a complex shear dynamic stiffness and dynamic stiffness recovery after a large strain amplitude:

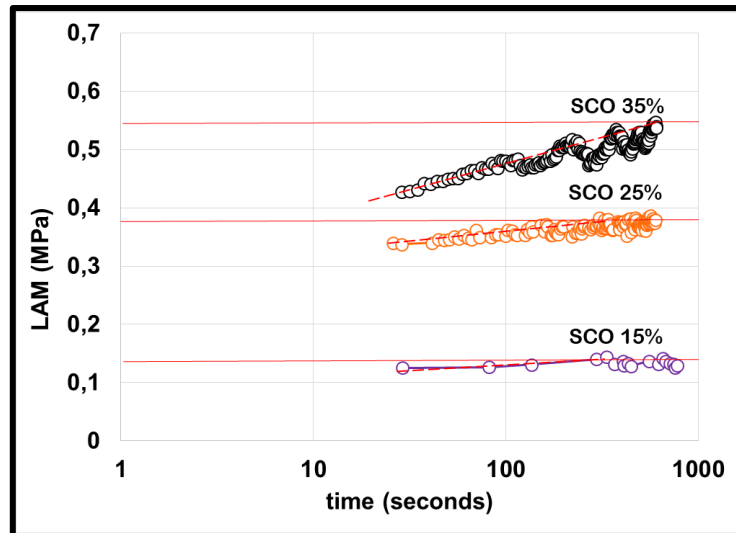
- after the FIRST cycle the stiffness immediately returns to the starting point for each Static Compression Offset.



Dynamic stiffness recovery

- After the FIFTH cycle there is not a sudden immediate return of the stiffness to its initial value, but there is a temporal latency.

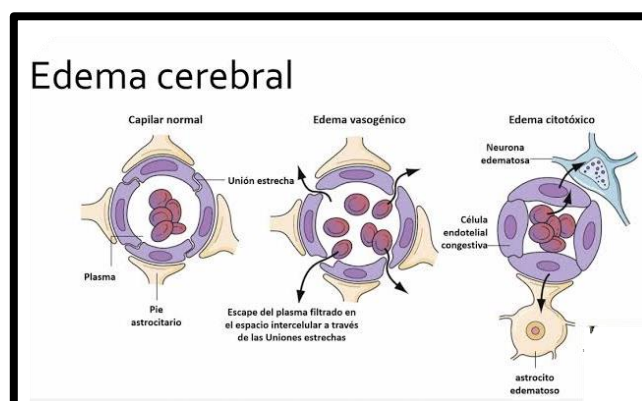
In particular, with increasing the offset preload both the temporal latency and the speed of recovery increase.



Trend of temporal latency and the speed of recovery

Probably there are some explanations of the aforementioned points: after five cycles there are a greater effect of cytotoxic and vasogenic oedema due to the addition of insults in the various cycles and a greater extravasation of water from the intra to the extracellular compartment.

Latency is probably due to a more serious oedema with extravasation of extracellular water which then also restores the initial dissipated water.



Schematic physiology of cerebral edema

In conclusion we can assert that microstructural architecture of our brain affects its macrostructural response.

6. DESIGN OF OUR INSTRUMENT

6.1 OBJECTIVE

Our goal is to devise a tool capable of overcoming the limitations of the current technological solutions available for retraction previously discussed. The design choices, made on the basis of an in-depth bibliographic research on the case study, were implemented and supported through finite element simulation (FEM), the results of which were appropriately interpreted.

6.2 MATERIALS

The first design choice even before geometry was that of the material. As already illustrated, there are numerous references in the bibliography to the opacity of the current spatula retractors, which therefore do not allow the visualization of the retracted tissue necessary to monitor the retraction and prevent any damage. We therefore opted for a transparent polymeric material and the choice immediately fell on polycarbonate (PC).

Polycarbonate is an amorphous thermoplastic polymer that is characterized by its transparency, resistance to temperature and impact. Thanks to these characteristics, polycarbonate is classified as a technical polymer (polymer with high physical-mechanical properties).

For these reasons it is used in artifacts where safety is essential, for example it is used in motorcycle helmets or when high temperature sterilization is required, such as in some hospital objects.

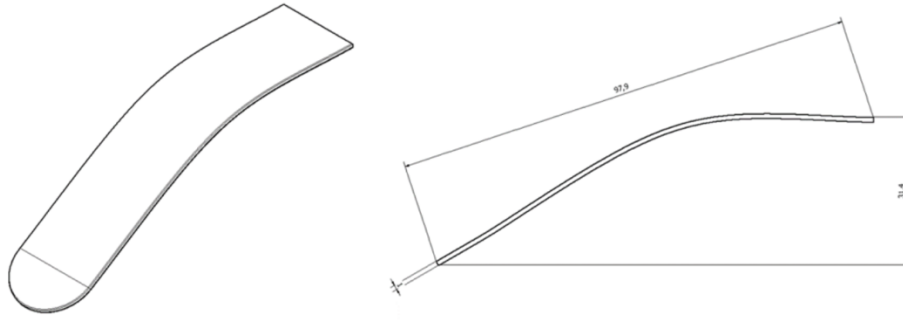
Against a higher cost, however, polycarbonate stands out for its high thermal resistance (the glass transition temperature is around 150 ° C versus 110 ° C for PMMA) and superior impact resistance.

6.3 GEOMETRY

The choice of geometry must satisfy two particular requirements. The first is due to the choice of material: we pass from an elastic modulus in the order of 200 GPa (steel) to that of polycarbonate, 2.2 GPa. It is therefore necessary to compensate for the loss of stiffness of the material with a stiffening of the section.

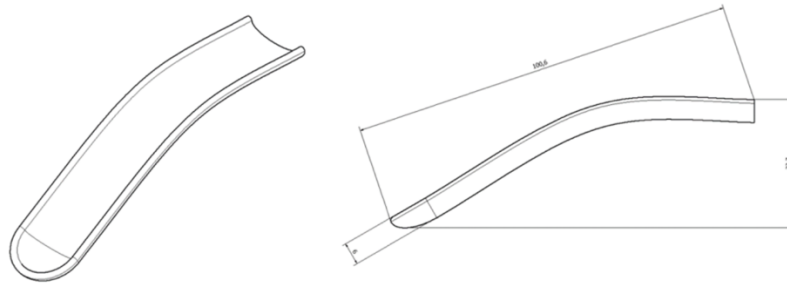
The second concerns the contact surface with the fabric. Since, as previously reported, numerous studies attributes to the flat geometry of the current retractors the cause of the high number of injuries reported during retraction. The geometry must be able to follow the deformation of the fabric as closely as possible without generating high pressure gradients.

The following geometry has therefore been defined starting from the dimensions of the metal spatulas currently in use and on the market.



Common geometry of the spatulas currently present on the market

Similarly, the geometry of a metal alloy spatula currently used in the operations was replicated in a CAD model. The resulting CAD model was then used to compare the performance of the "new" spatula with the "old" one.



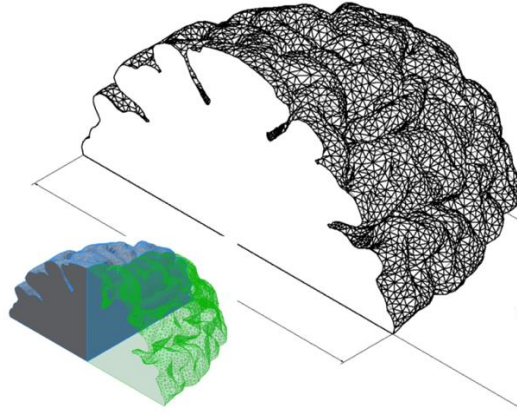
Geometry of the retractor made, the "U" section involves a considerable stiffening of the section, especially in bending. Dimensions in millimetres. The width of the spatula is 22mm.

Both CAD models were imported into an FEM simulation program where different analysis configurations were devised to highlight the performance improvement as well as to study the stresses and strains associated with the retraction.

6.4 SIMULATED GEOMETRY

Brain

In addition to the CAD models of the two spatulas already described, a CAD model of a section of a real brain obtained from a scan was used.



CAD model of a section of a real brain

The simulations carried out with this geometry were particularly demanding: the very complex geometry prevented the software from finishing the analyses by interrupting them in advance.

However, the results obtained were not sufficient to compare the shrinkage obtained with the two different spatula geometries.

To overcome this limitation due to the computational complexity connected to the geometry, the CAD model of the brain was replaced with a hemisphere, the simulation of which was then decidedly easier.

The choice of such a simple geometry also allowed to eliminate another complexity, consisting in the configuration of the retraction: how to make the spatulas come into contact with the brain in order to obtain comparable results that are also valid for any other contact configuration. The configurations between spatulas and hemispheres were found to be simple to define uniquely for both and the results were deprived of the strong variability due to the geometric complexity of the brain.

The simulations with the brain model that managed to complete were however used to ensure the reliability of the results of the analyses of the analogues with the sphere.

6.5 FEM ANALYSES

Finite element analysis, also known as FEM, is a numerical calculation technique that allows you to find solutions to complex problems that are difficult to solve analytically.

Therefore, some software is used that discretize reality and carry out a set of differential equations that describe the behaviour of the case study object, for example static, dynamic, thermal analyses,

etc. The solution obtained is an approximate result, the result of multiple repetitions of calculation, but it represents reality in a more than acceptable way.

The discretization of the element (or elements) takes place through the creation of a mesh, which is a grid of 2D shapes (triangles, squares) or 3D (tetrahedra, cubes) depending on the options selected. Each mesh element has nodes and edges shared with the adjacent elements and the calculations on the equilibrium equations are performed on these nodes.

The definition of the mesh is a crucial phase as it influences the quality of the results: it is not possible to define the quality or the size of the mesh in advance, because it varies according to the element to be analysed, therefore it tends to thicken it in the areas of greatest interest or where there is high variability, for example of a load. Next it is necessary to introduce the properties of the materials that make up the model.

Generally, simple materials with linear isotropic behaviour are used, i.e. where the correspondence between stress and strain is linear. For these types of material, two elastic constants are needed: the elastic modulus and the Poisson's ratio.

By selecting models corresponding to increasingly complex materials, it is necessary to gradually define an increasing number of parameters up to the possibility of providing the entire experimental curve to the software.

It is then necessary to define and place constraints, displacements and loads applied to the components of the analysis. Proceed by selecting the affected nodes of the mesh (corresponding to the stressed or constrained areas of the piece) and defining the type of constraint or load applied to them.

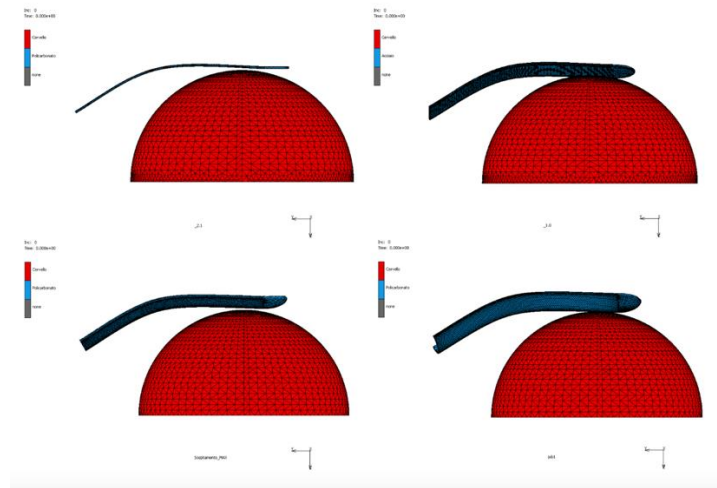
In the case of several components that come into contact with each other, it is necessary to specify to the software the contact bodies and what type of interaction develops between them. For example, the "contact type" used in the simulations reported below has been defined as "touching": a contact that allows translation and relative rotation without interpenetration of the two bodies.

Finally, it is necessary to indicate to the software which results we want to obtain from the simulation, these can be both scalar and vectorial and are calculated for each element of the mesh.

6.6 SIMULATIONS

The following simulations have been set up to investigate the development of pressure on the brain surface during retraction.

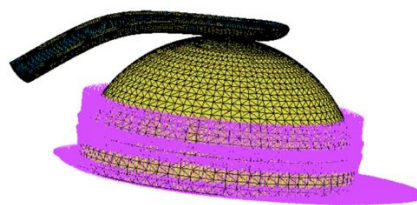
Two different retraction conditions have been devised: one with a straight spatula and one with a slightly inclined spatula (15 °). Both were forced to move the same way.



Starting from the top left, Spatula-A Straight, Spatula-A inclined, Spatula-B Straight, Spatula-B inclined.

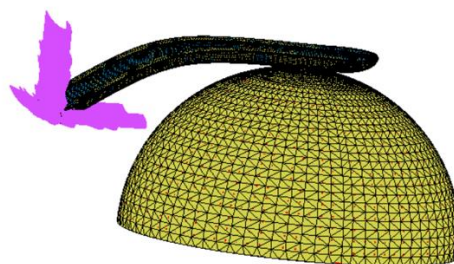
The boundary conditions used in the analyses are now presented. The proposed images relate to the constraints, displacements and loads applied to the models of a single simulation (Spatula-B straight) presented as an example.

The hemisphere, representative of the brain, is constrained to the base as shown in the figure. Beside the definition of the constraint: all the possible translations and all the possible rotations of the nodes are blocked.



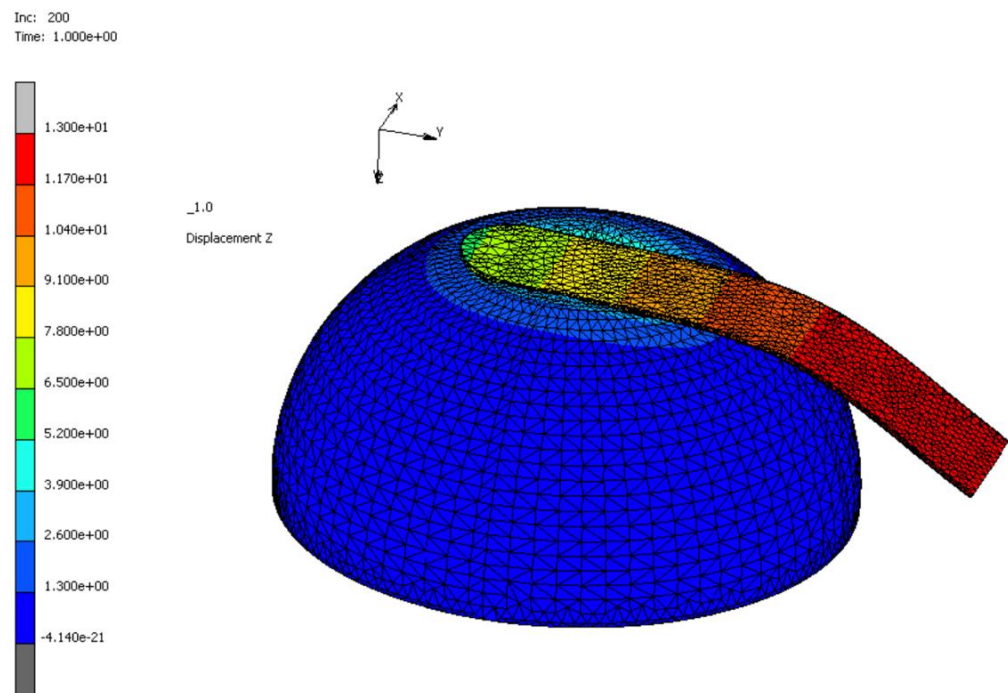
constraint display

The spatula is instead constrained on the nodes highlighted in the figure. All rotations and translations are set equal to zero except for the displacement in Z.

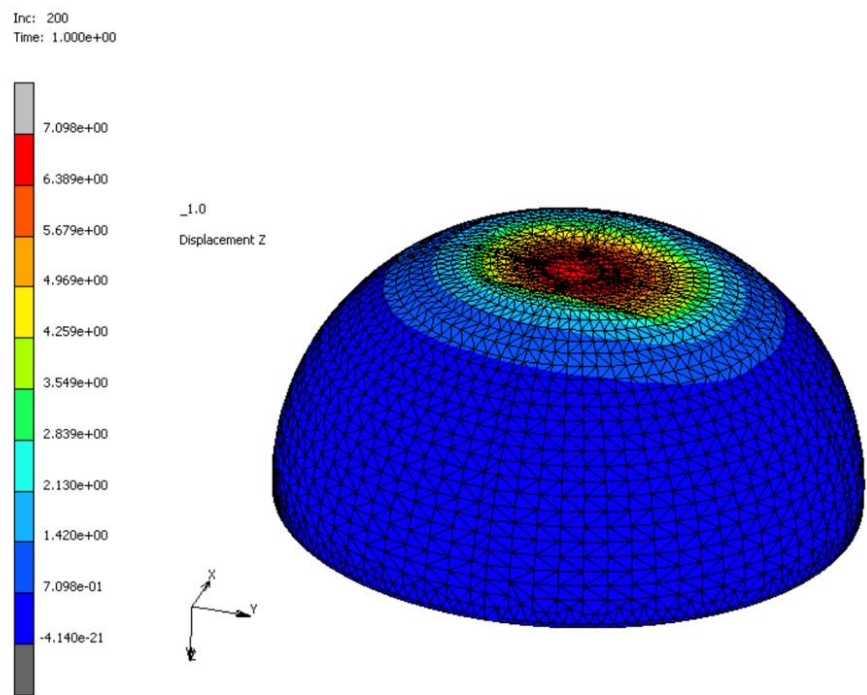


display of the constraint just defined.

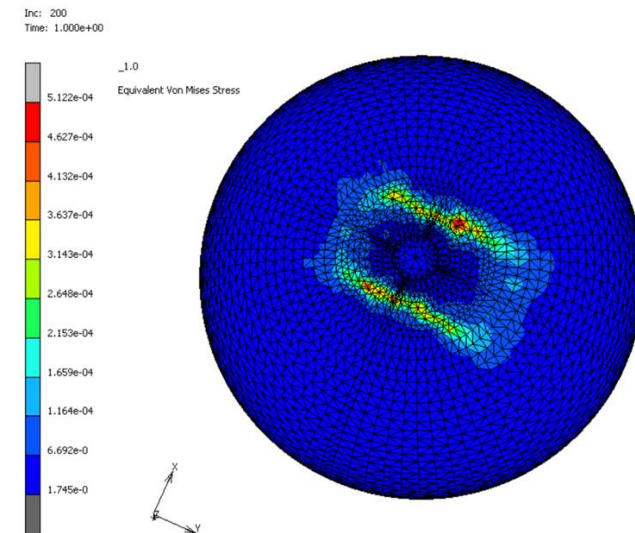
Spatula A. flat configuration



Report 1 Spatola-A Piatta, Spostamento Z.



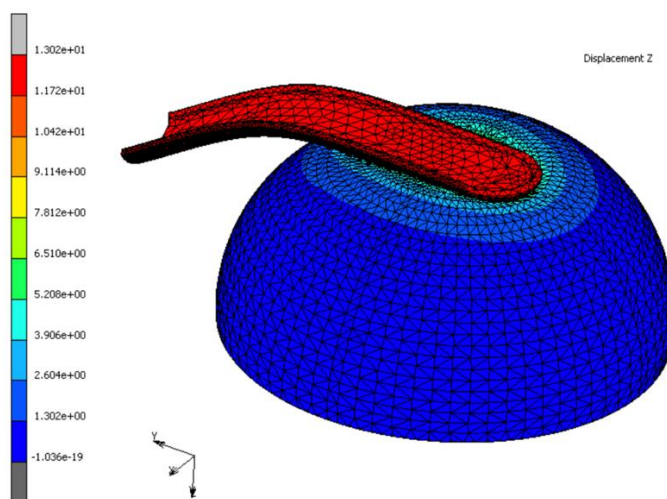
Report 2 Spatola-A dritta, Spostamento Z. Rimossa la spatola per visualizzare meglio la retrazione.



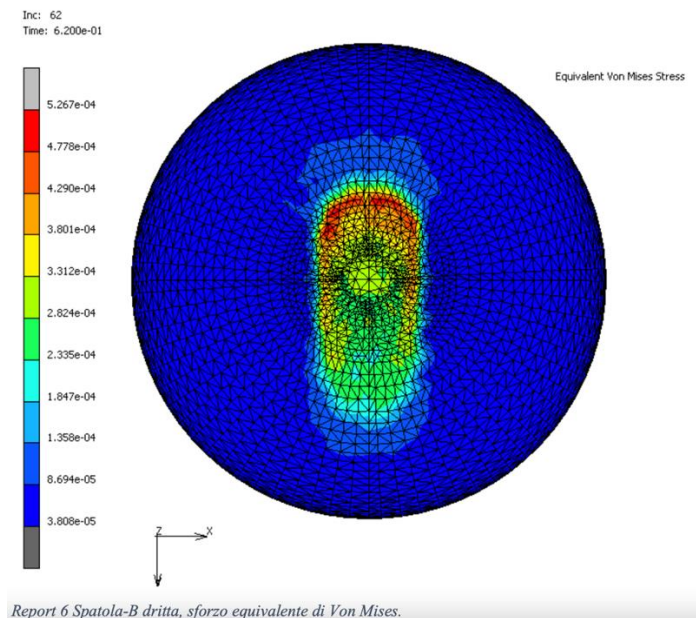
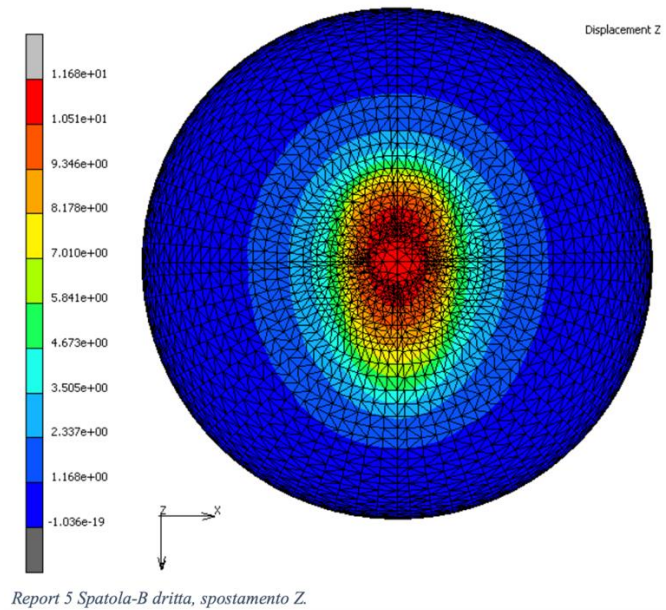
Report 3 Spatola-A dritta, sforzo equivalente di Von Mises.

In report 1 it is clearly visible that the spatula-A made of polycarbonate is not sufficiently rigid to be able to efficiently retract the brain. In fact, we see in report 2 that the maximum displacement value in the Z direction p is just over 7 mm compared to a displacement impressed on the spatula of 12 mm (1 mm gap). In report 3 you can see the distribution of efforts through the Von Mises effort. The distribution is not uniform at all, the fabric near the edge is stressed with maximum values that exceed 500 Pa.

Spatula B. flat configuration



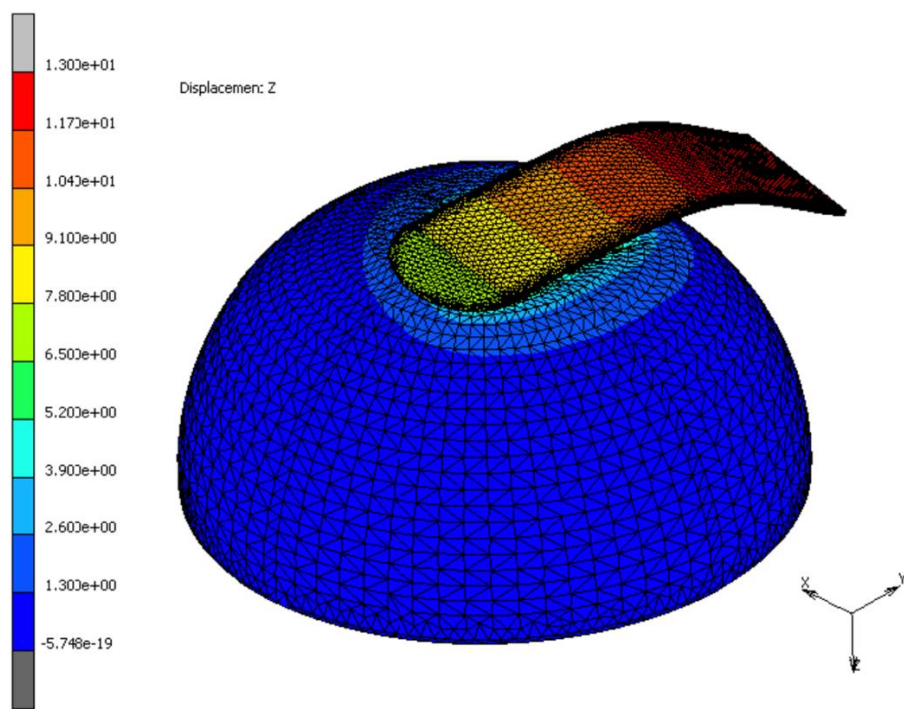
Report 4 Spatola-B dritta, spostamento Z.



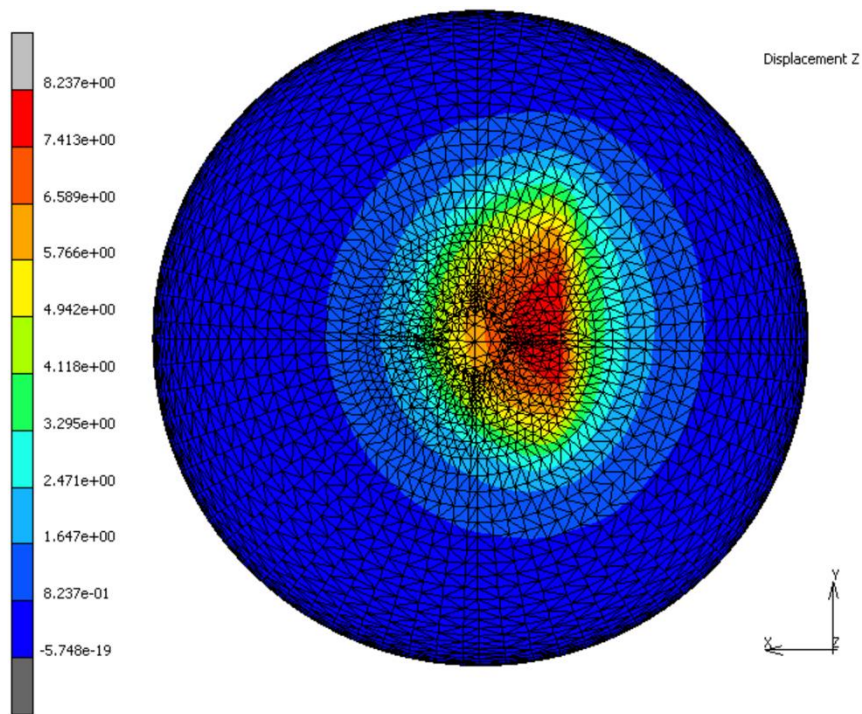
Report 4 shows how the spatula-B, thanks to the modification of the section, has stiffened and does not present the visible signs of bending that can instead be seen in the spatula-A in report 1. The displacement of the brain occurs homogeneously (report 2), and with values close to 12 mm, further proof that the spatula is able to withstand the load without deforming too much. In report 6 we analyse the efforts of Von Mises, the fabric is homogeneously stressed with values that slightly exceed 500 Pa. Value comparable with the maximum scale of report 3, for the spatula-A. this comparison, however, must take into account that the spatula-B achieved a maximum retraction of 11 mm against a retraction conducted by the spatula-A of 7 mm.

The spatula-B is therefore able to effectively retract the fabric, generating less and more distributed stresses in the fabric itself than the spatula-A.

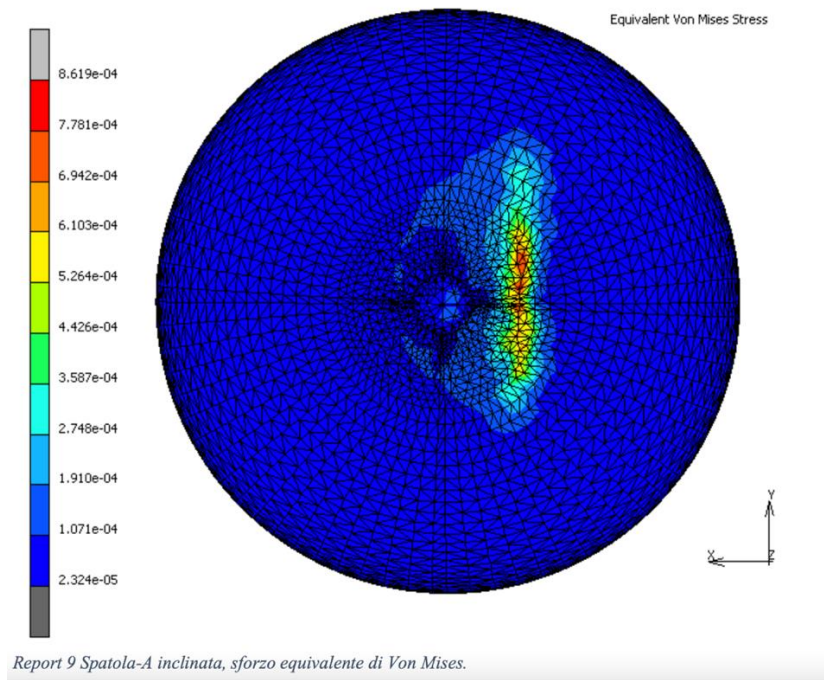
Spatula A inclined at 15 °



Report 7 Spatola-A inclinata, Spostamento Z.



Report 8 Spatola-A inclinata, spostamento Z.



Report 7 presents the same criticalities of the spatula-A observed in report 1.

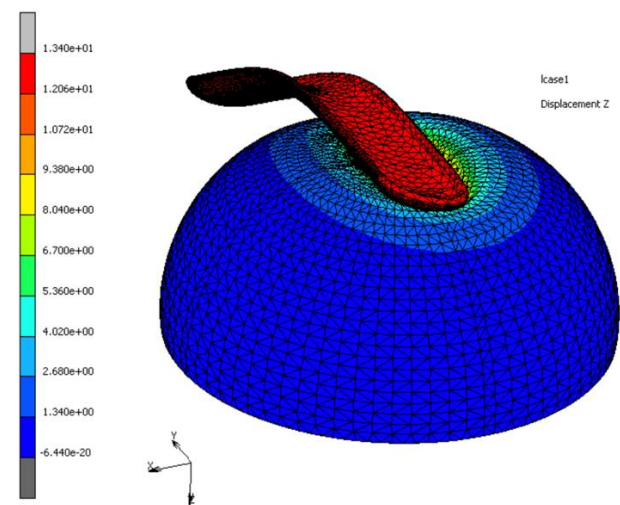
In report 8 the displacement generated by this configuration leads to a maximum displacement of less than 9 mm, maximum values concentrated at the point of contact with the side of the spatula.

As anticipated by the focused displacements observed in report 8, report 9 shows a high concentration of efforts in the area of contact with the spatula. Efforts reaching maximum values of 860 Pa.

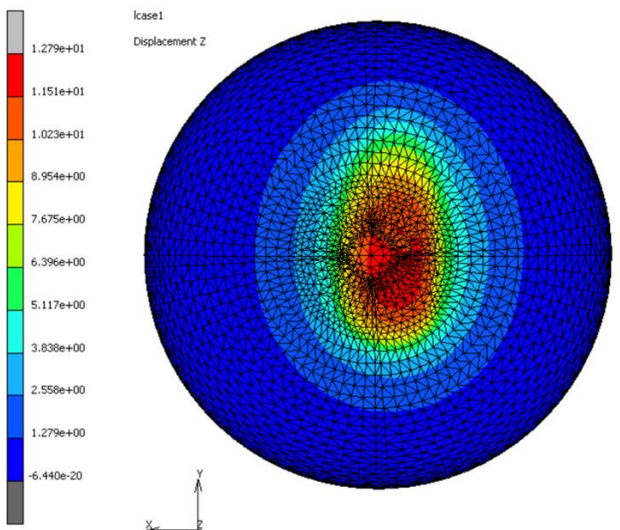
Compared to report 3 (relative to the simulation performed with spatula-A, straight), in report 9 I register an increase in the maximum effort from 500 to 860 Pa compared to a similar movement (report 8 and report 2).

We therefore have a worsening of the performance of the A-geometry spatula if the retraction is applied with an angle of incidence (in the simulated case 15 °) with respect to the fabric.

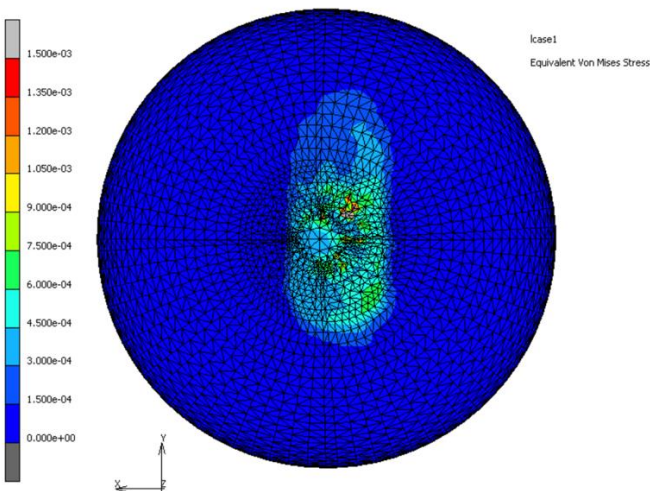
Spatula B inclined at 15 °



Report 10 Spatola-B inclinata, spostamento Z.



Report 11 Spatola-B inclinata, spostamento Z.



Report 12 Spatola-B sforzo equivalente di Von Mises.

Also in this configuration the spatula-B shows adequate stiffness, in report 10.

Report 11 (displacement Z for the inclined spatula-B) is comparable with the homologous report 5 (displacement Z for the straight spatula-B) both in the distribution and in the maximum values (to avoid problems related to the contact of the two bodies during the analysis the straight spatulas were started with 1mm of detachment from the hemisphere, it is therefore necessary to consider legitimate the displacement difference in the order of 1 mm).

Report 12 is difficult to interpret due to some nodes that return very high point values (unreliable, the result of analysis anomalies). The scale was then manually imported and shown to be isolated nodes. The rest of the surface has values in the order of 800 Pa. Value, once again comparable with the analogous report 9 (Spatula-A inclined, equivalent stress of Von Mises) but in the face of a higher displacement.

Therefore, even in an inclined configuration, the spatula-B has better performance in terms of retraction obtained with the same stress peaks.

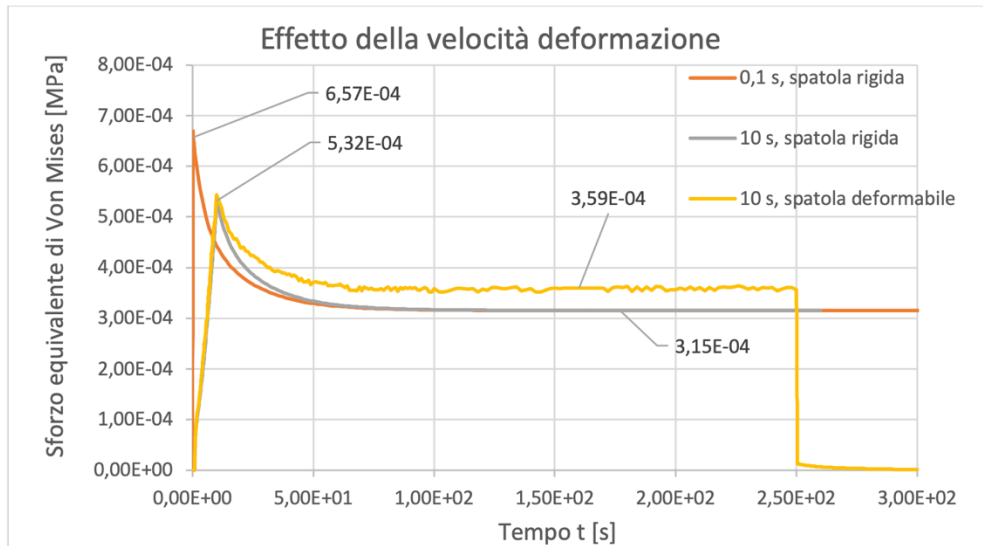
Finally, by comparing the displacement and stress reports of the spatula-B in straight and inclined configuration (reports 5-6, 11-12) we obtain on the one hand 11mm of retraction with peaks of 520 Pa on the other, a retraction of 12.7 mm with stress peaks of 800 Pa. We observe a slight worsening of the ability to retract while keeping the stress values low.

EFFECT OF DEFORMATION RATE

The "Spatula-B flat" analysis has been modified in the calculation settings in order to obtain data relating to the maintenance over time of the deformation applied by the spatula.

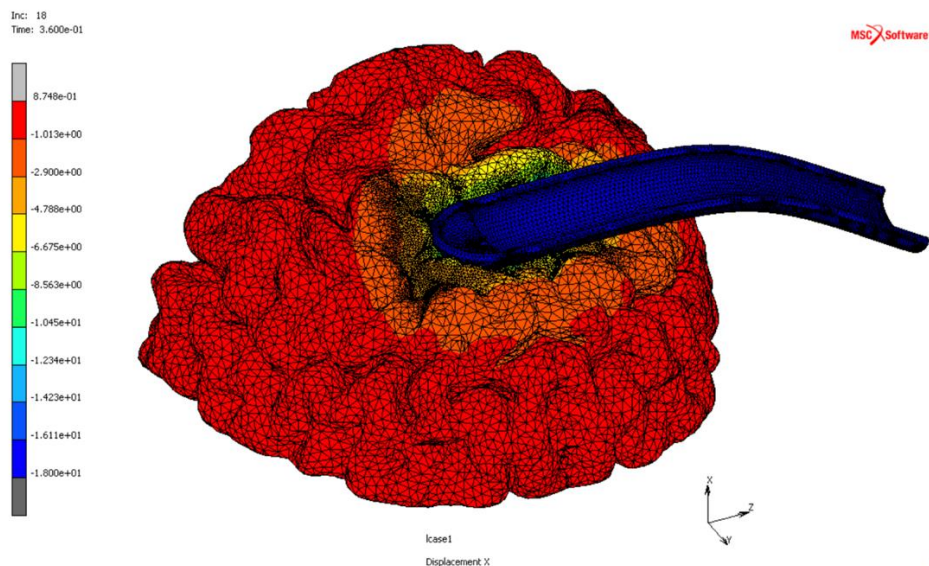
For simplicity of analysis, the Von Mises equivalent stress values were evaluated at the node at the apex of the hemisphere.

By applying the same displacement (10 mm) in two different time intervals, we observe effort peaks significantly greater than those necessary to maintain the retraction. This particular effect is due to the viscous component of the material (which we have defined as viscoelastic).

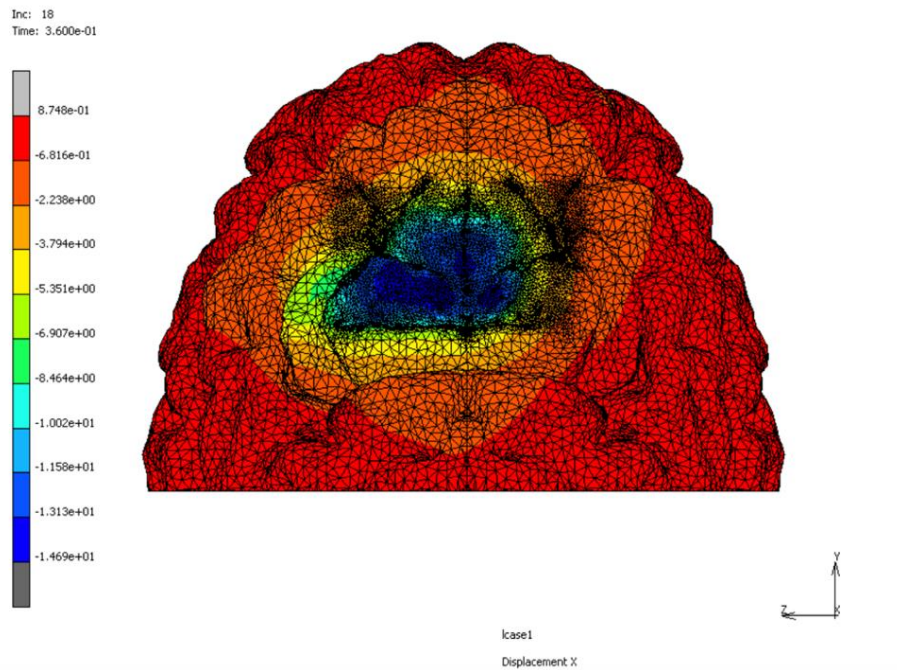


This graph shows the Von Mises stress values recorded over time at the apex of the hemisphere in a "straight B spatula" simulation where a displacement of the spatula equal to 11 mm was set and maintained over time. The rigid and deformable captions in the legend refer to the type of constraint application. The yellow curve also shows a strain relief that is performed by removing the spatula.

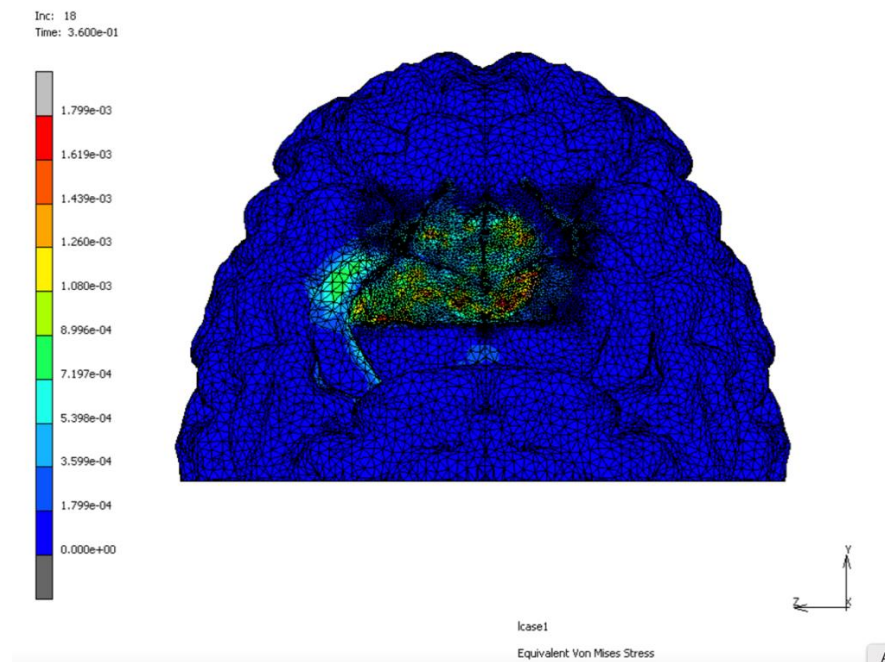
6.7 FEM ANALYSIS WITH BRAIN MODEL



Spatula-B Brain, X shift



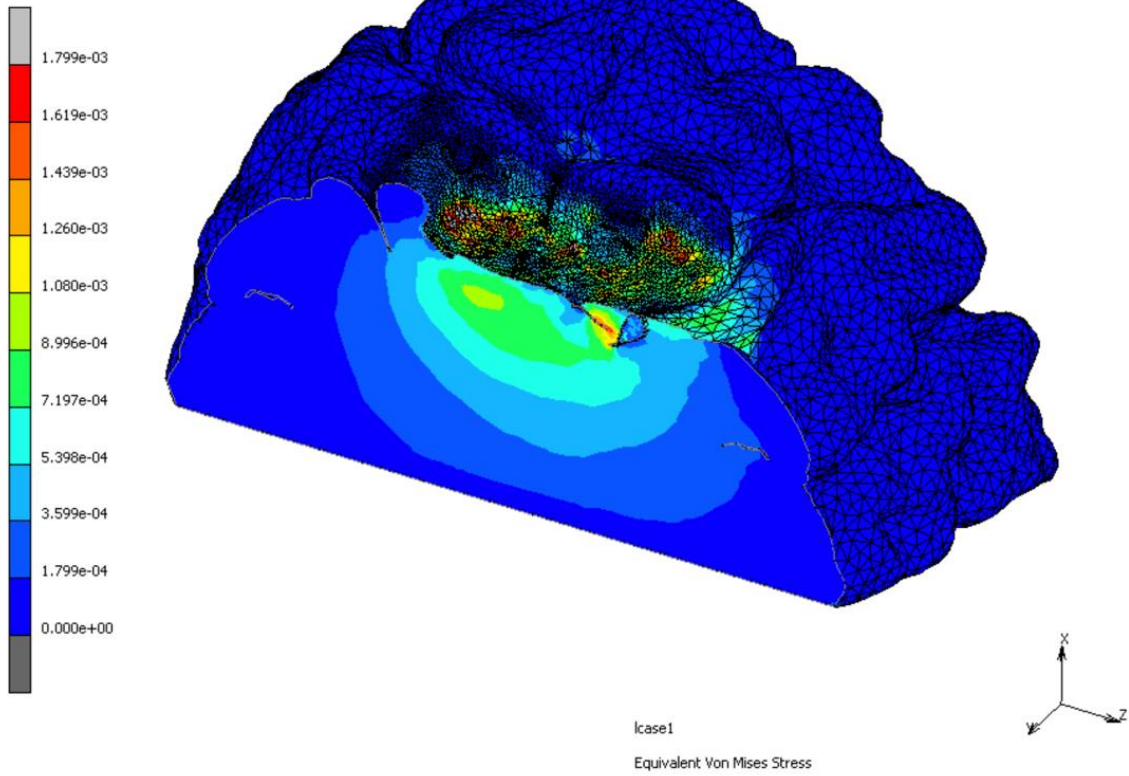
Spatula-B Brain, X-shift, imprint.



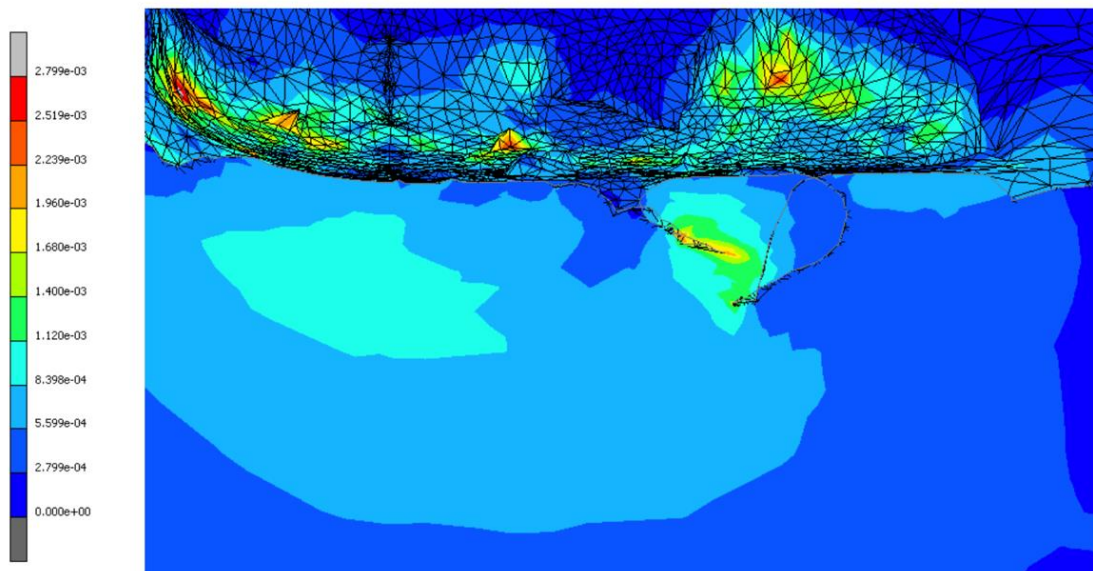
Spatula-B Brain, Von Mises equivalent effort, imprint.

These simulations were obtained by simulating the CAD models of the spatula-B and the symmetrically duplicated brain model in order to have a larger surface on which to test the retraction. The brain mesh has been superficially thickened in the area where the spatula will apply pressure. The results are comparable in terms of maximum values and distribution with the results obtained from the simulations with the sphere.

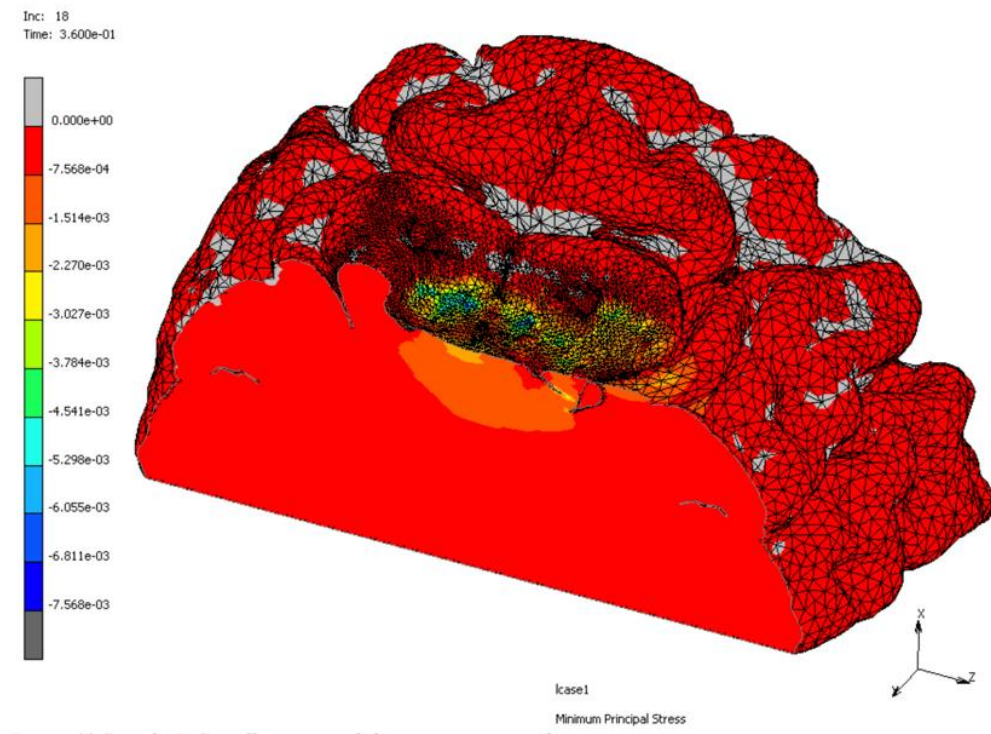
Inc: 18
Time: 3.600e-01



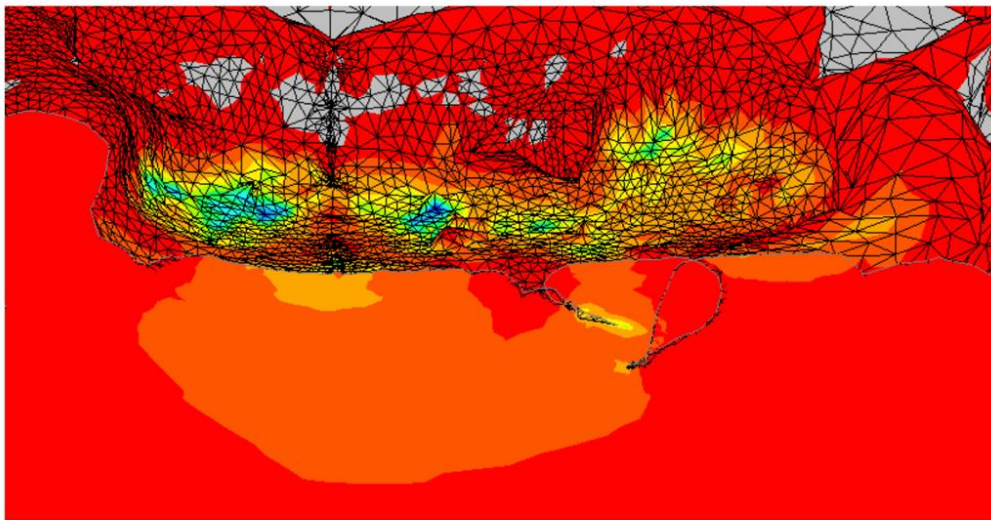
Spatula-B Brain, Von Mises equivalent effort sectioned impression.



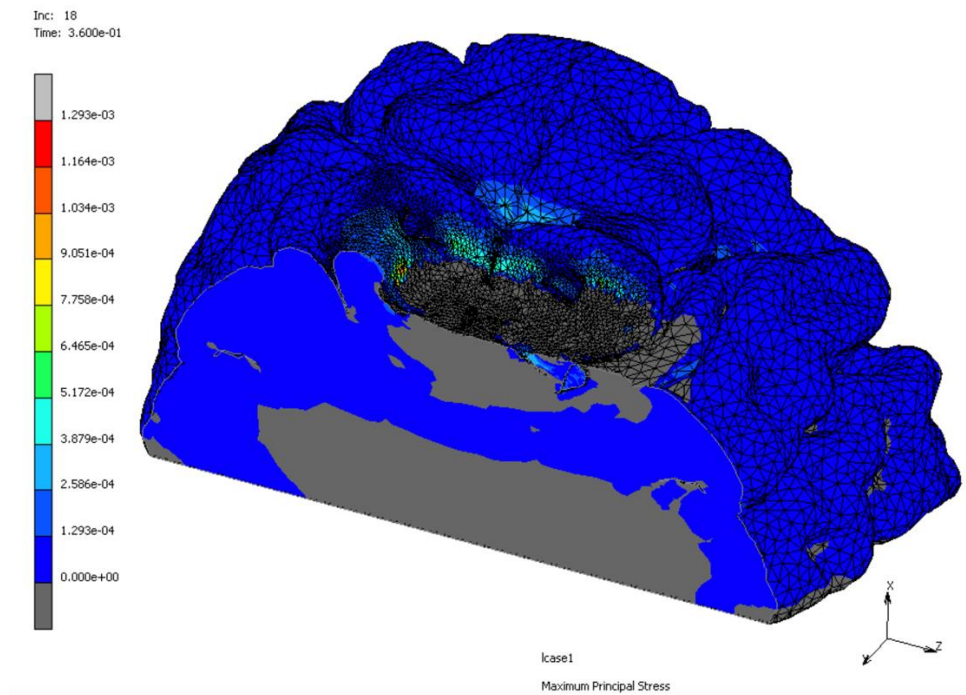
Spatula-B Brain, Von Mises equivalent effort detail



Spatula-B Brain, minimal principal deformation.



Spatula-B Brain, minimal principal deformation. Detail



Spatula-B Brain, Maximum main effort

7. MEASURES

One of the goals of this study was to find an effective method for measuring retraction pressure that could be as simple and versatile as possible so that it could be used later in normal neurosurgical procedures. First of all it was necessary to choose the type of sensor to be used, a piezoresistive sensor was evaluated among the availability proposed by the market.

7.1 PIEZORESISTIVE SENSORS

Piezoresistivity is the characteristic that all materials have of varying their electrical resistance when they are subjected to the action of external forces.

The application of a force leads to the modification of both the number of charges and the average mobility therefore an axial stress, compression or traction, leads to the variation of relative resistivity.

Repeatability

Repeatability is the degree of agreement obtained when measuring the same by measuring under the same measurement conditions. Thus it allows to define the sensor's ability to respond in a constant and consistent way to an identical force applied repeatedly.

Linearity

Linearity refers to the type of response that the sensor offers when it is stressed. In particular, it highlights how much the measurement system varies from an ideally perfectly linear response. (Improve linearity with calibration)

Hysteresis

The hysteresis is the signal difference that occurs when loading and unloading cycles are applied under the same force. For applications where the force is static or monotonous increasing, the hysteresis effect is obviously minimal. When there are increases or decreases in the same measurement phase, the hysteresis can be important and is not always compensated by the calibration.

Time drift

Time drift is the variation of the signal outgoing from the sensor when a constant force is applied for a significant period of time. If the sensor is subjected to a constant load, its resistance will tend to decrease over time, thereby increasing the output. The drift can be considered and compensated for in the calibration phase by applying the loads within time intervals similar to those being measured.

Temperature effect

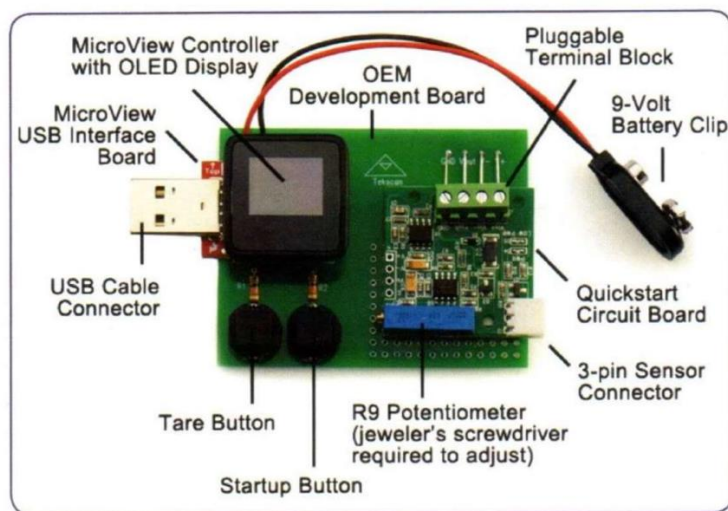
The temperature and its variation led to the modification of both the Gauge factor (GF) and the value of the nominal resistance, this dependence is quantified by the thermal sensitivity.

It is essential to operate at temperatures as close as possible to those in which GF is obtained.

Gauge Factor: fundamental quantity for this type of transducer; it relates the variation in electrical resistance with the deformation undergone by the material.

7.2 MISURE SYSTEM

For the combination of cost-effectiveness, ease of use and portability, the FlexiForce OEM Development Kit from the American company Teskan has been identified as a suitable measuring tool. It consists of a development board, two FlexiForce sensors, a USB key containing the acquisition software and a USB A-B cable. The development board is composed in turn of a MicroView USB Interface Board and a MicroView Controller with an OLED screen, two buttons (calibration and ignition), the Quickstart Circuit which presents the potentiometer, the block for the terminal connection, the 3-pin for sensor and connection for 9-volt battery. The Arduino components convert the analog signal coming from the Quickstart Circuit Board into a digital signal that can be viewed directly on the display or acquired through a computer and dedicated software.



Composition of the acquisition card that makes up the Development Kit

FlexiForce sensors are flexible and particularly thin printed circuits that can be easily integrated into different applications, in fact thanks to their properties they are able to measure forces between almost any type of surface and in different environments.

The sensor consists of a double substrate composed of a polyester film, or polyamide in the case of sensors for high temperature applications. A conductive material, silver, and a pressure sensitive ink

layer are placed on both substrates. An adhesive is then used to colaminate the two substrates and form the sensor. To complete the sensor and in order to be able to put it in contact with an electrical circuit there are three connectors, of which the two external ones are active, while the control unit does not carry an electrical signal. As already described, the sensor behaves like a variable resistance, in particular when it is not under load there is a resistance greater than 5 megaohm while when a force is applied the resistance decreases. There are several possible ways to use a FlexiForce sensor, one of which is to incorporate it into a force-voltage type circuit. It is then necessary to carry out an appropriate calibration to relate the electrical quantity with the physical one, depending on the specific circuit some variations can be made to vary the sensitivity of the sensor. In our case the quickstart circuit board took care of the translation of the signal.

Of the various sensors available, the A201 model was chosen as it allows for a length comparable to that of the reference retractor so as not to reduce its ergonomics and interfere with the retraction procedures. The A201 is a thin and flexible piezoresistive force sensor that is on the market in four different lengths, from 50.8mm to 190.5mm, and three force scales, 4N, 111N and 445N. For the reasons of ergonomics and practicality just mentioned, it was decided to use the 190.5 mm sensor, the choice of the force scale required an investigation in the literature regarding the typical forces involved.

As has already been said in the literature (3; 6; 13) it emerges that the critical retraction pressures are in the order of 25 mmHg; starting from this data and knowing that the diameter of the sensitive area is $d = 9.53 \text{ mm}$, it is possible to trace the force values involved.

First it was necessary to obtain the surface of the area through the formula:

$$A = \pi \frac{d^2}{4} [mm^2]$$

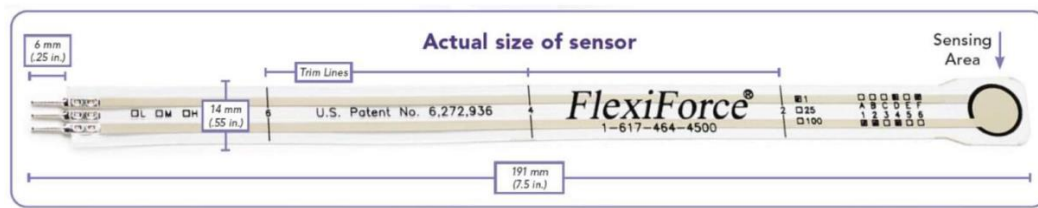
Thus obtaining a value of 71.33 mm.

Subsequently, the values in mmHg were converted into units of measurement for the pressure of the international system, that is Pascal. Knowing that $1 \text{ mmHg} = 133.32 \text{ Pa}$, it follows that the pressures are of the order of 3500 Pa.

Thanks to this and the subsequent formula it was possible to obtain the typical force value F ,

$$F = \frac{A \cdot P}{10^6} [N]$$

Obtaining an F value of about 0.25 N and moving the choice towards the sensor with a full scale of 4N so as to have sufficient sensitivity and no fear of reaching the full scale by saturating the signal.



A201 sensor used during the tests with relative measurements.

An important phase is the calibration of the sensor with a uniform distribution of the forces and it is also important to perform the procedure at the same temperature in which the forces of interest will then be measured.



Positioning of the sensor on the retractor to obtain the retraction pressure values.

7.3 UpSim HYBRIDE SYMULATOR SYSTEM

As a preclinical phase, before testing our device on a corpse and in the clinic, we therefore used a special simulator: UpSim from the company UpSurgeOn s.r.l.

It is a hybrid simulator for neurosurgical training consisting of two parts: the app needed to create the augmented reality environment and the physical simulator.

The physical simulator is further divided into the base, the augmented reality marker and the one that is the fulcrum of everything, that is the box containing the model of the chosen brain area. There are three possible approaches: pterional, temporal and retrosigmoid depending on the different needs.

The anatomical model was created by the combined work of neurosurgeons and 3D designers and validated in its accuracy through more than 1000 hours of study.

In addition to providing the possibility of exercising the surgeon's manual skills, in working with delicate structures even during the use of the microscope, it allows to offer mental exercise thanks to both the simulation component and the modularity and anatomical fidelity that allows you to explore and visualize the deeper structures of the brain.

7.4 TESTS PROCEDURES

In order to investigate the most suitable method for measuring the retraction pressure, various tests were carried out on the UpSim simulator with a pterional approach.

The first phase of the tests focused on investigating the applicability of the TekScan measurement system, already presented, to the type of retraction required and to the reference spatula. This preliminary investigation covered the assessment of the calibration phase, the identification of the calibration and conditioning masses, the training in the retraction necessary to understand the operational needs, and only after this were measurements carried out with actual retractions.

As mentioned, the A201 sensor was used, with a length of 191mm similar to that of the retractor, and with 4N full scale.

Knowing the literature values that should have been found, about 25g, a series of masses was sought that could cover a neighborhood of this magnitude for the calibration phase. Three batteries of 11g, 23g and 50g were identified that could be suitable not only for the relationship between the reciprocal masses, but also for a uniform distribution of the mass in its own volume and simple geometry. Given the need to have a uniform load distribution on the sensor and the excessive size of the larger batteries, use was made, temporarily, of EVA thermocolla to adapt the surface of the batteries to that sensitive area.

Having identified and modified the three masses, calibration was carried out, the company suggests calibrating the instrument on a smooth surface and on the same surface on which the measurements will be made, this was not possible as the spatula, due to use prolonged, it had residual deformations that led it to sway during loading and to give variable and untrue readings. Therefore, the calibration was performed on a surface similar in roughness and hardness, but flat and stable.

In each of the three tests, similar retraction forces between 50g and 80g are reached. The peaks present are attributable to disturbances that have led to inadequate readings more than to real forces since for the type of tests the presence of impulsive forces is difficult, the peak is within a time window of 0.1 s.

The need to have masses that can exceed 80g was important, this is necessary to be able to carry out a correct conditioning to have at least 120% of this mass. For this reason, the set of masses presented in figure 3.14 has been identified as suitable for the purpose. It is composed of six different masses, one of 10g, two of 20g, one of 50g, two of 100g and one of 200g. As anticipated, we made use of the masses of 20g, 50g and 100g.

8. LABORATORY TEST OUR INSTRUMENT

8.1 RETRACTION TESTS

In order to identify a clear target for the retraction, a yellow and red glass ball with a diameter of 16mm was used, positioned in the simulator as shown in the figure.

The tests were performed by positioning the sensor A201 in the so-called proximal position or, as shown in figure 4.1, with the terminal part of the sensor in contact with the final part of the spatula, this is because intuitively and as confirmed by the study in the area in the greater the depth, the higher retraction pressures are found, therefore more dangerous.



a) position of the ball as the target of the retraction. b) proximal position of the sensor on the spatula.

8.2 SIMULATOR TESTS

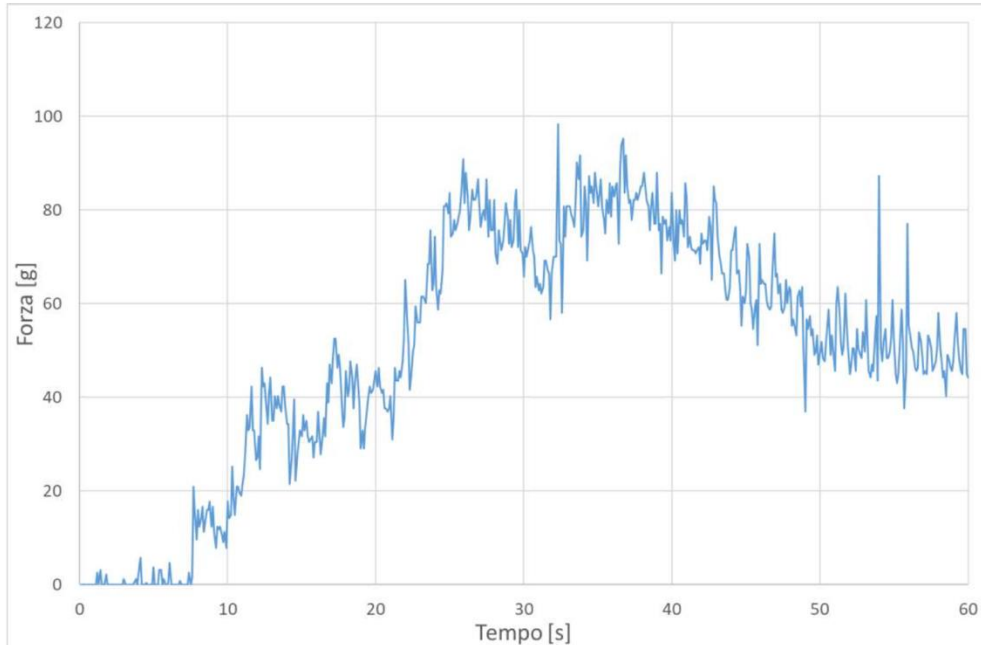
The first tests conducted in this configuration were performed by an operator with no medical and surgical experience, this to evaluate, once again, how the entire system can respond to an inexperienced hand such as that of a student who has to be trained.

Before presenting the data, it is important to specify that they are shown with units of measurement in g, since calibration necessarily leads to obtaining this unit. Given the configuration, the conversion from grams to mmHg is rather simple and direct, in fact $1\text{g} = 1,053\text{mmHg}$ is obtained.

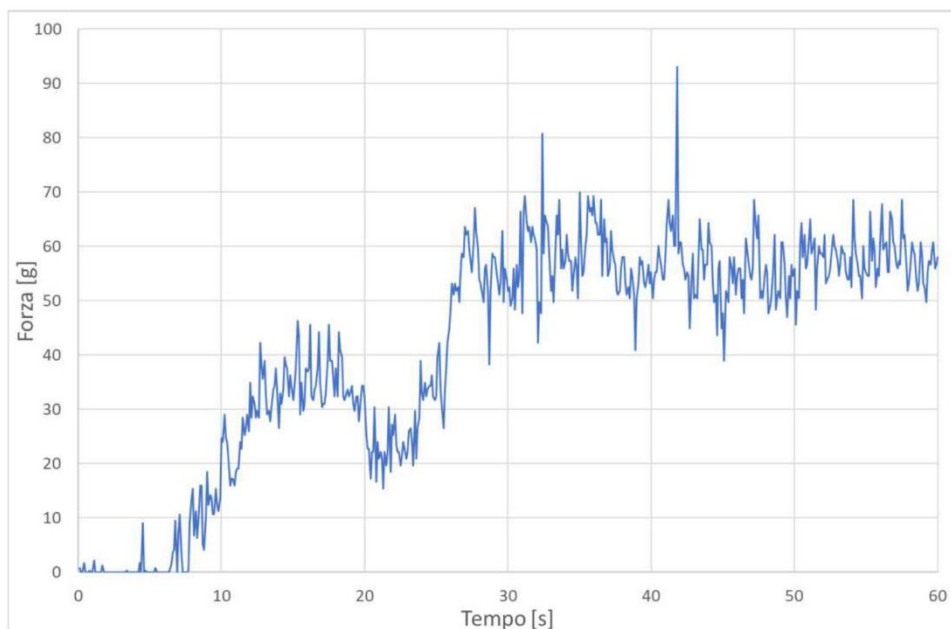
The following graphs (figures 4.2, 4.3 and 4.4) show the results of three retraction tests carried out by the inexperienced operator whose operating procedure was to start by inserting the retractor in the known position of the ball and try to expose it for about 10 mm, maintaining the retraction until the end of the test.

The graphs show comparable trends with a gradual growth of the load and then it is kept relatively constant, there is no manifestation of relaxation of the efforts, if not slightly in the first graph, this may be caused by the operator who reports that he has tried to maintain the constant pressure and

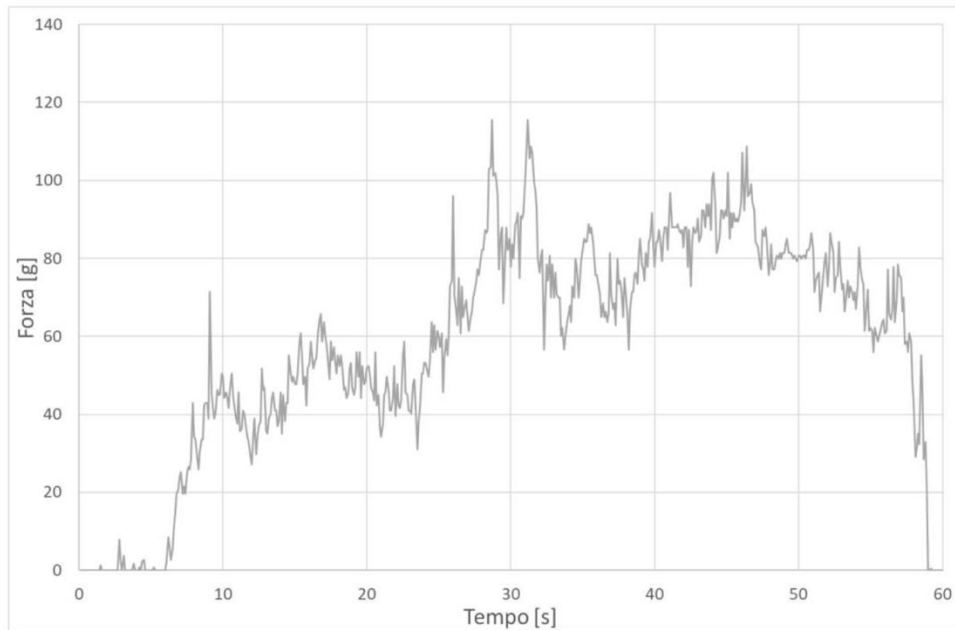
focusing less on maintaining the same retraction. In the second graph there are high peaks, about 120g, probably deriving from operator shortcomings. However, it is good to repeat that the time scale is in the tens of seconds so that these peaks are included in a few seconds or even tenths of seconds.



Retraction test 1 performed by an inexperienced operator.



Retraction test 2 performed by an inexperienced operator.



Retraction test 3 performed by an inexperienced operator

The force values deriving from the five tests performed were measured, considering the values in the region that most likely presented a plateau so as to be significant than an average. The values are shown in table 2.1.

	Prova 1	Prova 2	Prova 3	Prova 4	Prova 5	Medie
<i>Valore medio [g]</i>	72,0	44,5	79,7	64,3	56,91	63,5
<i>Dev. Std [g]</i>	10,7	10,6	11,3	16,02	5,90	13,5
<i>ΔTempo [s]</i>	28	39,1	31,7	30,8	33,8	32,68
<i>Min [g]</i>	36,9	16,0	55,9	38,90	38,24	37,2
<i>Max [g]</i>	98,3	92,4	115,4	116,19	93,11	103,1
<i>Delta [g]</i>	61,4	76,4	59,5	77,29	54,87	65,9

Force values measured during the retraction tests on the simulator

As already mentioned, the graphs presented refer respectively to test 1, test 3 and test 5.

From the data in the table, it can be seen that there is a certain variability in the averages of the retraction forces, in particular test 2 and test 3 are at the extremes for minimum and maximum values, respectively. This result is not surprising and does not affect the validity of the measurement system, in fact there is a clear influence of the intrinsic variability of the test which, being performed by a

human hand, cannot be easily eliminated, moreover the time interval considered is quite wide. and you can see, from the graphs, how there can be even important variations, but which must be taken into consideration.

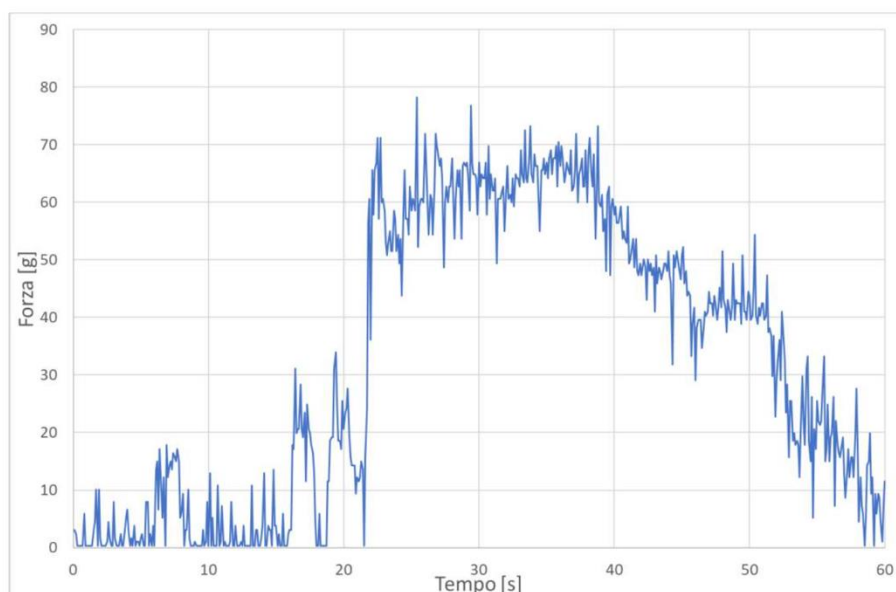
That said, the mean value of the five tests remains in line with the literature data reported by Evins et al.

Following the tests carried out by the inexperienced operator, the validity of the system and the force values were investigated in the event that an experienced neurosurgeon operates the retraction.

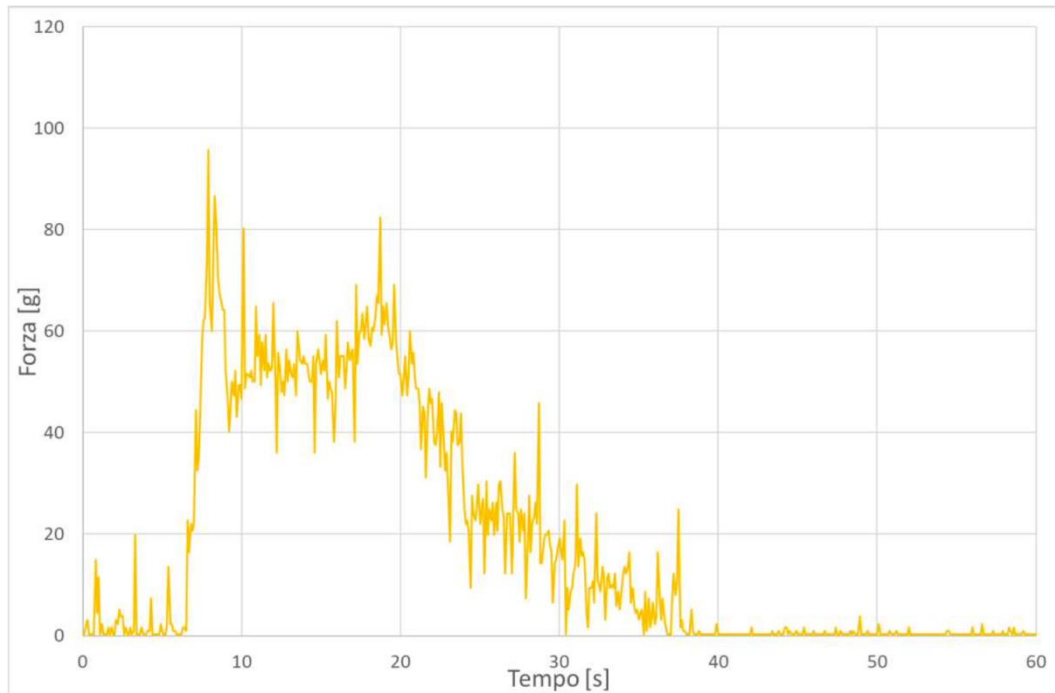
During the test, what would happen in the case of a real operation was simulated, i.e., not knowing the exact location of the lesion, in our case, it is necessary to perform exploratory retractions to locate it. Once the lesion has been identified, a minimal retraction is performed to allow aspiration of any cerebrospinal fluid. This retraction was evaluated in relation to the size of the bead and was evaluated to be approximately 8 mm.

The graphs relating to two retraction tests performed as described above and with the sensor positioned proximally are presented below.

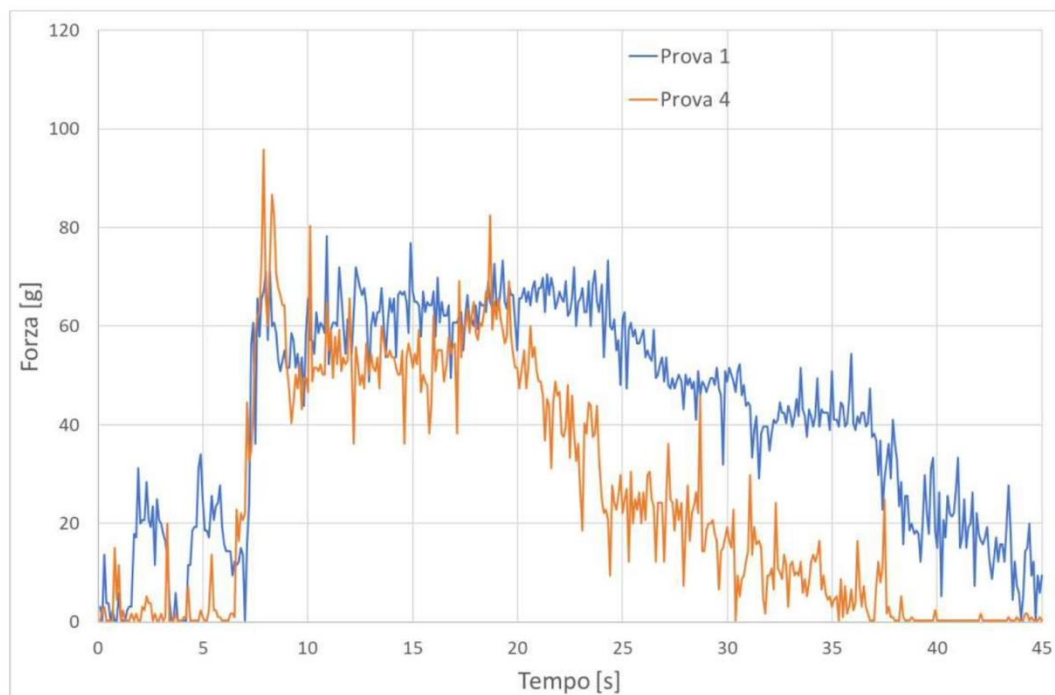
The first graph highlights some peaks prior to the major growth and subsequent maintenance of the load, these are due to the exploration phase for identifying the target. From the experience of the neurosurgeon these peaks are not correctly representative of the forces at play which should be greater than what was detected, this discrepancy is attributable to the anatomy of the simulator which has some cavities in correspondence with the sensor which therefore cannot correctly detect the forces at stake.



Retraction trial 1 performed by an experienced neurosurgeon. Relaxation of efforts is shown.



Retraction test 2 performed by a neurosurgeon. There is a strong relaxation of efforts



Comparison between the relaxation occurred in the tests shown in figure aforementioned

In both tests there is a rapid growth of the load when the lesion is identified, this increase is followed after a few seconds, 15/20 s, by an evident relaxation of the efforts. This relaxation causes the retraction effort to cancel itself out in a short time, once again about 15 and 20 s, this allows to drop below the critical loads reported in the literature of about 25g, thus avoiding generating permanent damage.

In the third graph the two graphs were compared, moving the results of the first test along the time axis, in order to better compare the two different relaxations, it is clear that in both tests the relaxation is similar indicating a constant response to the same solicitation.

Relaxation should be further emphasized during a real operation as cerebral fluid is removed and this leads to a reduction in the volume of the brain parenchyma resulting in relaxation.

From these tests we can however affirm that the simulator actually manifests a behaviour very close to that of the human parenchyma. As with the tests carried out by the inexperienced operator, we wanted to investigate the force values obtained during retraction, given the greater operating precision and the presence of relaxation, in this case the values considered were those included between the moment in which retraction suitable for viewing has been reached and the subsequent 12.5 s.

The results of these acquisitions are shown in the following table.

	Prova 1	Prova 2	Prova 3	Prova 4	Media
<i>Valore medio [g]</i>	61,62	69,2	71,4	56,30	64,6
<i>Dev. St. [g]</i>	6,27	13,1	17,3	9,35	11,5
<i>min. [g]</i>	36,07	45,2	15,0	36,07	33,1
<i>max [g]</i>	78,19	101,4	105,6	95,74	95,2
<i>Delta [g]</i>	42,12	56,2	90,6	59,67	62,1

Summary of the strength values obtained by the neurosurgeon.

The graphs shown refer to the data of the tests identified with the name Test 1 and Test 4.

From the data shown in the table we can see how, once again, the average strength values reflect what emerges from the literature. Compared to the tests performed by the inexperienced operator, there is a lower variability of the average values which is reflected by a lower standard deviation.

Once again there are high peaks and the difference between the maximum and minimum values, it is always valid, as can be seen in the graph of test 4, that the peaks refer to short intervals of time, sometimes so short that they can be attributed to wrong readings and therefore it could be useful to carry out a more in-depth analysis to purge them of the signal and the readings.

8.3 SPECIMENS TESTS

Following the tests carried out on the simulator, it was possible to perform similar tests on a fixed cadaveric model so as to verify and evaluate the retraction pressure values on a human model.

Before presenting the data obtained from the tests carried out on the cadaveric sample, it is interesting to deepen the study proposed by Evins et al.

The thesis work produced by Evins et Al. Concerned the investigation of the difference in retraction pressure between tubular and traditional retractors, these pressures were calculated by measuring the average force of the minimum retraction necessary to obtain an adequate visualization of the target within cadaveric models. Subsequently there was also a visual and qualitative assessment of the retracted tissue to assess the presence of possible damage.

The study investigated different neurosurgical approaches to cover the widest possible variety of medical practices and possibilities. Approaches were standard supraorbital, middle fossa, retrosigmoid, infratentorial supracerebellar, interhemispheric and transcortical, performed on three cadaver heads without arteriovenous injection. A further division was based on the relative position of the retractor, i.e., with the retractor between the parenchyma and the dura, the parenchyma and the skull or inside the parenchyma.

The target for each different facility was defined in such a way as to provide one that could guarantee a similar standard for each procedure.

The study is even more interesting because a measurement system similar to the one we used to be used, in fact the Teskan company's FlexiForce Economical Load & Force Measurement System was used.

Each different approach was performed six times, three with the tubular retractors and three with the spatula. The spatula used was 229mm long and 3mm to 13mm wide, while the tubular retractors were 12x8mm wide and 70mm long in all approaches except in the retrosigmoid and median fossa case where a 12x8mm and 30mm long retractor was used respectively. a retractor 17x11mm and 70mm in length.

Force measurements were performed after obtaining visualization of the lesion and attaching the retractor to the support arm.

The mean retraction distance MRD of the parenchyma was measured using a surgical ruler at the opening point of the skull, which allowed to cover the non-retracted and fully retracted tissue.

In each approach, measurements were performed on two different points of the retractor, proximal and distal, where proximal is the closest point of contact between the tissue and the spatula and vice versa the distal one. As regards the tubular retractors, the pressure values were evaluated in four positions, proximal and distal on both the upper and lower sides, in the event that the retractor was

placed between the parenchyma and the dura or inside the parenchyma itself, in the approaches where the retractor was in contact with the skull, two measuring points were used, proximal and distal, positioned on the side in contact with the retracted parenchyma. Each measurement was performed four times.

At the end of each measurement and the subsequent removal of the retractor thanks to the use of a surgical microscope, the study visually investigated the presence of damage such as, deformity of the cortical tissue, collapse of the vessels, damage to the cortical surface, lacerations of the cerebral parenchyma along the surgical corridor and at the edge of the retractor.

The retraction values were first measured as retraction force and subsequently converted into pressure expressed as millimetres of mercury (mmHg).

Each approach was performed bilaterally on all three samples, leading to a total of 36 retractions, 18 with the use of the spatula and another 18 with tubular retractors. In each approach, the retraction pressure was measured effectively when the minimum retraction necessary to visualize the structures considered as target was reached. The MRP was found to be 56.93% lower in the case of the use of tubular retractors, obtaining a pressure of 37.89 ± 5.18 mmHg (range from 17.00 to 49.72 mmHg) compared to that relating to the traditional retractor where it is a mean total pressure of 87.98 ± 10.80 mmHg was detected (between the values of 54.92 and 118.71). As far as the proximal measurements are concerned, the reduction described is 59.27%, the pressure passed, in fact, from the average values of 100.96 mmHg in the case of the spatula to average values of 41.12 mmHg using the tubular retractor. This reduction is confirmed by the distal data which are described to be 58.25% lower in the case of tubular retractor, where a pressure of 33.31 mmHg is reported, while using the spatula a pressure of 75.00 mmHg was obtained. In any case, it is shown that there is a clear and significant reduction in pressure between the proximal and distal measurements.

The study showed that in each approach a significant reduction in pressure values was obtained when using the tubular retractors. The greatest reduction shown was in the case of supraorbital and transcortical approaches in which a reduction of 66.82% and 69.05% respectively was obtained. In the supratentorial approach, the study found a reduction of 60.92%, from 118.71 ± 2.77 in the case of spatulas to 46.39 ± 1.27 mmHg using tubular retractors. In the middle fossa approach, there is a reduction of 56.73%, again with a tubular retractor, going from 114.91 mmHg to 49.72mmHg. The same result is shown in the retrosigmoid approach where it goes from 93.47 mmHg to 42.11 mmHg, equal to a reduction of 54.95% using tubular retractors. The minor reduction occurred in the case of the interhemispheric approach, where the pressure was reduced by 17.57 mmHg equal to 28.44%.

Distribution of the retraction pressure of the spatula

As shown in the graph mentioned above, the study highlighted significant differences between proximal and distal MRPs in all approaches except interhemispheric and transcortical. In particular, the greatest reduction is obtained in the supraorbital and retrosigmoid approaches where a distal pressure is obtained which is, respectively, 54.92% and 34.01% lower, while in the case of the middle fossa and supracerebral approaches the proximal pressure is of the 22.00% and 8.98% greater.

This shows that there is a concentration of force at the tip of the retractor.

Distribution of the retraction pressure of the tubular retractors

The thesis shows how in the case of retractors the pressure difference along the axis is generally lower, in fact, a significant variation is obtained in the interhemispheric, middle fossa and retrosigmoid approaches. In particular, in the last two there is a difference of 10.63% and 16.57% respectively, while in the first the greatest reduction is shown, which is 52.95%. It is interesting to note that in the transcortical approach the greatest pressure is found in the distal section of the retractor and that in the approaches in which the sensors were positioned on opposite sides of the retractor, no significant pressure difference was obtained.

Pressure distribution: differences between spatula and tubular retractor

By comparing the data relating to the distal or proximal pressure distribution between the traditional retractor and the tubular one, Evins et al. show how in each approach the decrease in retraction pressure is confirmed using the tubular retractor. The minimum difference is obtained in proximal pressures during the interhemispheric approach, while the maximum differences are exchanged between middle fossa and supracerebral in the proximal and distal case respectively.

Retraction pressure as a function of the position of the retractor

Another fact that the study considers and highlights is the difference in pressure obtained according to the position of the retractor, i.e., whether it was positioned between the parenchyma and the dura, between the parenchyma and the cranial bone or inside of the parenchyma. As mentioned in each approach the retraction pressure is lower using a tubular retractor, this is confirmed by the data differentiated according to the position. In particular, it is interesting how the lower pressure data are obtained using a tubular retractor positioned between the parenchyma, average pressures of 16.75 mmHg are reached which are 69.05% lower than using a spatula and is the reduction greater in this analysis.

Average retraction distance

Given the geometry and the practice of use, the retraction achieved with the use of retractors was equal to the span added to the thickness, leading to a total of 9mm in each approach except in the case of a middle pit where it was necessary to use a retractor wider tubular and having a retraction of 12mm. Using the spatula in the study, it was necessary to obtain variable retractions greater than those achieved with tubular retractors, in particular the average retraction varied from 15.5 to 29.5 mm, or on average 10 mm greater equal to 49.94% increase compared to tubulars.

Retraction damage analysis

Both using the spatula and the Evins et al. Tubular retractors. found tissue deformities which in most cases were found to be slightly less than the mean retraction. Given the nature of the brain tissue, this study also shows how it returns to the position prior to the retraction within 10 minutes from the end of the retraction itself. The vessels along the surgical corridor were found to be compromised, however, given their non-perfusion, it was not possible to determine their collapse as they were not physiologically accurate. The study shows how damage to the cortical surface was present in both groups. In the case of tubular retractors, it was noted that the tissue entered the lower opening in three cases during the transcortical approach. Using the spatula damage to the cerebral parenchyma in the form of lacerations was noted in three procedures during the middle fossa and transcortical approaches and once during the supraorbital approach, in each of these the damage was found to be at the edges of the spatula.

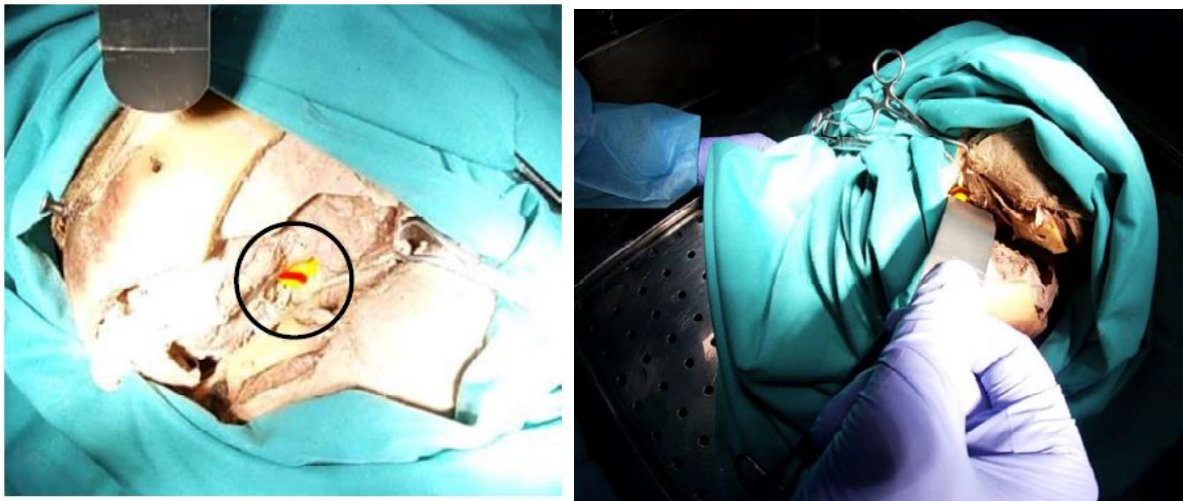
Summarizing what was reported by the study, it is evident that the average retraction pressure is less than 50mmHg or 57% when using a tubular retractor and not a spatula. In all cases, using the spatula or tubulars, the distal pressure was lower than the proximal one. When using the spatula, maximum pressure values of a single reading of 150 mmHg were reached, while using the tubulars they never exceeded 65 mmHg. With both types of retractors, the transcortical approach produced the lowest retraction pressure value. Given the static nature of the geometry of the retractors, the minor is easily explained standard deviation obtained, 12.70 mmHg compared to 26.44 mmHg using the spatulas. This may be attributable to the significant difference in retraction distance between the use of the spatula and the tubular retractor which allows a 50% reduced retraction. There were no differences in pressure between the sides of the tubular retractors. In 39% of cases of spatula retraction, laceration of the cortical tissue was noted.

Test methods and results

The tests were performed in the Anatomy Laboratory of Brescia on a cadaveric head previously subjected to a fixing process.

The preliminary procedures necessary for the correct use of the measurement system were carried out in the same way as already described, once again the sensor was first conditioned with the mass of 100g and subsequently linearly calibrated at three points with the masses of 20g, 50g and 100g.

To obtain a clear retraction target, a ball very similar to the one used for the tests with the simulator was used, therefore with a diameter of 16mm, this allowed to evaluate the retraction according to the size of the ball and to obtain an average retraction. of 8mm. The marble has been positioned as shown in the figure underlying.

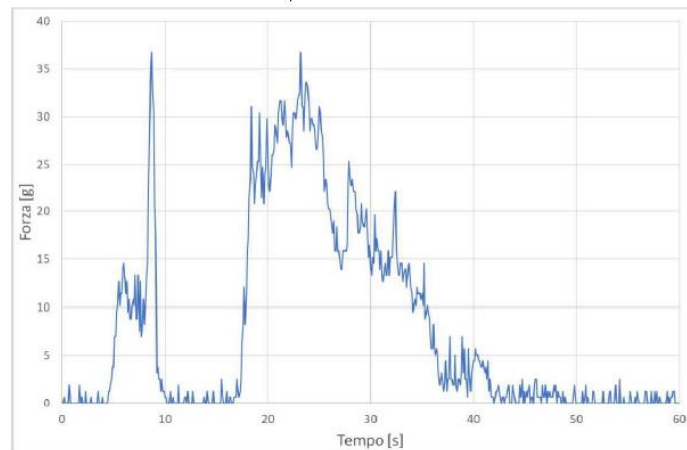


Tests on specimens

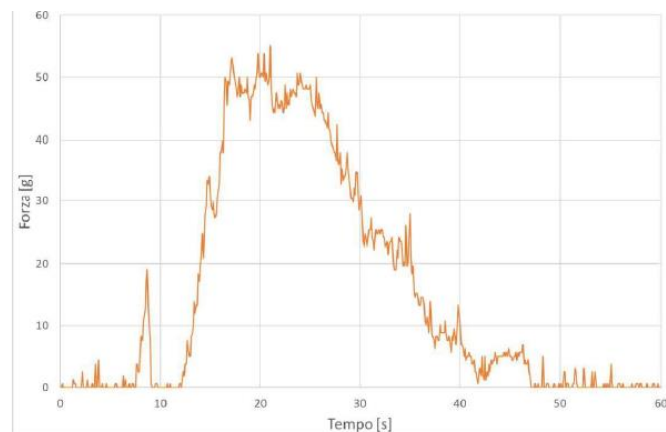
The graphs relating to the retraction tests performed without having any reference to the pressure values read by the instrument are shown below.

The two graphs show a similar trend although reaching different retraction force values, in fact in the first graph a force is reached at the point of maximum retraction of about 35g, while in the second it exceeds 50g. Despite this difference, the peaks given by the exploration phase are still present and are positioned at a similar instant of time, about 9s.

As in the case of the tests on the simulator, a rapid growth of the load is highlighted at the moment of retraction and after about 10 s, therefore less than in the UpSim model, relaxation begins to occur which for both tests ends by completely canceling the load in about 16s, from 26s to 42s, a time similar to that of the simulator test.

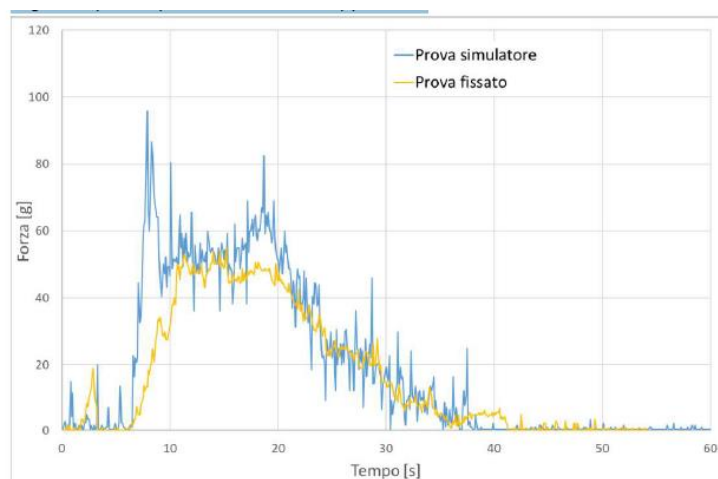


Retraction force values relative to the first test performed on the corpse.



Retraction force values related to the second test performed on the corpse.

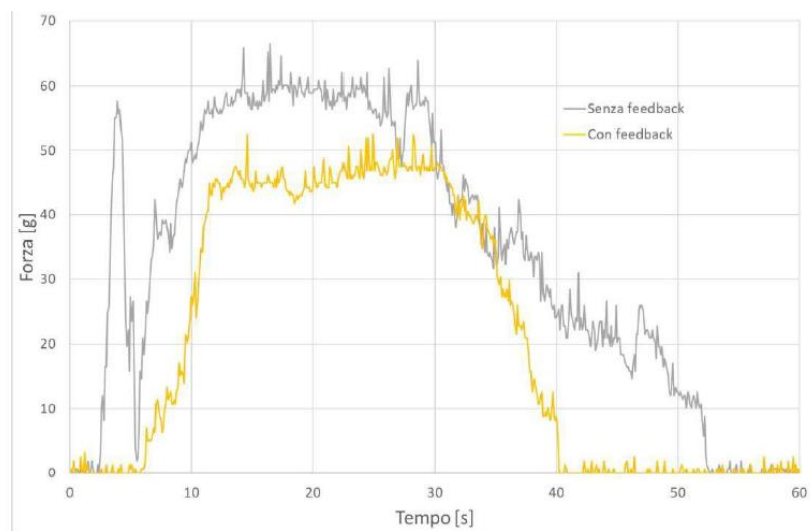
The graph underlying instead compares the tests performed on the simulator and on the fixed one so as to have a better view of how the behaviour of both is similar, in particular in the relaxation phase which follows a perfectly superimposable profile.



Comparison between the relaxation found on the fixed sample and with the UpSim simulator.

This demonstrates once again how the simulator is faithful to a human model making it effective and useful in the tests, this further validates the tests performed previously and those that will be presented later.

After the first two tests presented, the target was moved to the temporal area in order to evaluate whether a different position in the brain could modify the retraction values obtained. It is important to report what was highlighted by the neurosurgeon, namely that in the case of a real operation the approach used would have been different, exposing the temporal more and positioning the head so as to have easier access and probably lower retraction pressures than the one present in the fixed sample. The curves below show the two tests performed in this configuration. The first graph refers to the retraction performed without being aware of the force values that the instrument was detecting, while the second graph shows the results of the retraction performed by having a second operator who read and reported the force values to the neurosurgeon in real time.



Graphs relating to the tests carried out in the temporal area with and without an operator who provided feedback on the pressure value. It is noted that thanks to the feedback, the retraction forces are reduced.

As shown in the graphs, the presence of a feedback has effectively allowed the surgeon to remain below the threshold of 50mmHg while achieving an adequate visualization of the target. It is also possible to observe how in the case with feedback the pressure is maintained for a shorter time and the relaxation, while starting at a time similar to that of the case without feedback, is faster.

Therefore, the measurement system can be implemented in the case of daily use, but the possibility of a signal of exceeding the limit of force, visual or sound, convenient for the surgeon, is still missing, since this function cannot be delegated to a second. operator.

Table below shows the values relating to the four tests performed on the fixed sample relating to the linear section of the curve in which the retraction was maintained.

	Prova 1	Prova 2	No feedback	Con Feedback
Valore medio [g]	28,18	47,84	58,59	45,89
Dev. St. [g]	3,29	2,31	1,62	2,18
Min [g]	20,89	43,04	55,06	41,77
Max [g]	36,71	55,06	62,03	52,53
Delta [g]	15,82	12,03	6,96	10,76

Summary of the data relating to the retractions obtained on specimen

From the table emerges that there is an increase in the retraction force in retracting the temporal zone, this increase is however cancelled when there is an operator reporting the read values, in fact, as already seen from the graphs just presented, the value of average force is lower than that of test 2 and of the limit one, in particular a reduction is obtained with respect to not having feedback of 12.7g equal to 21.68%.

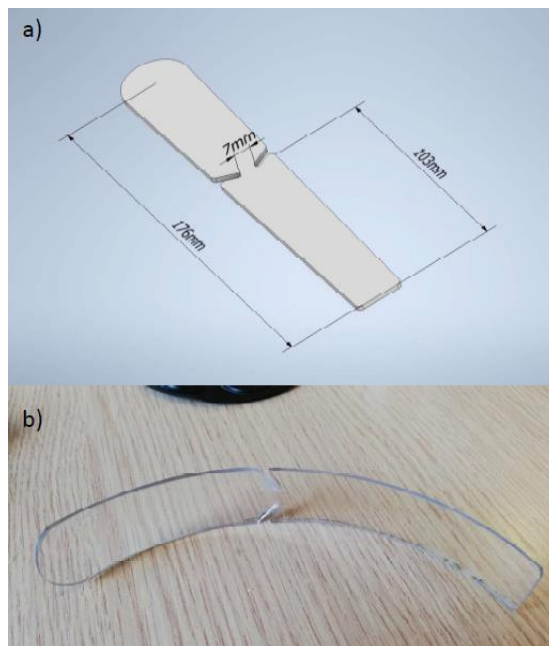
Comparing the values obtained with that reported by Evins et al. it emerges that they are in line with the values presented as regards the interhemispheric and transcortical approaches, approaches that have similarities with the experimental procedure followed during the tests on the fixed sample.

9. OUR DEVICES

9.1 TRANSPARENT SPATULA

In order to obtain the transparency required to view the retracted fabric, a polycarbonate spatula was created. In addition to ensuring high transparency, it has been designed in such a way as to avoid exceeding the critical retraction pressure value during its use. This was possible by creating the geometry presented in figure 5.1 as a CAD drawing. As you can see, the reduction to 7mm of section in the centre of the spatula, which ideally creates a handle, allows to reduce the compliance of the flap, providing the operator with greater sensitivity on the applied load and naturally avoiding reaching critical loads.

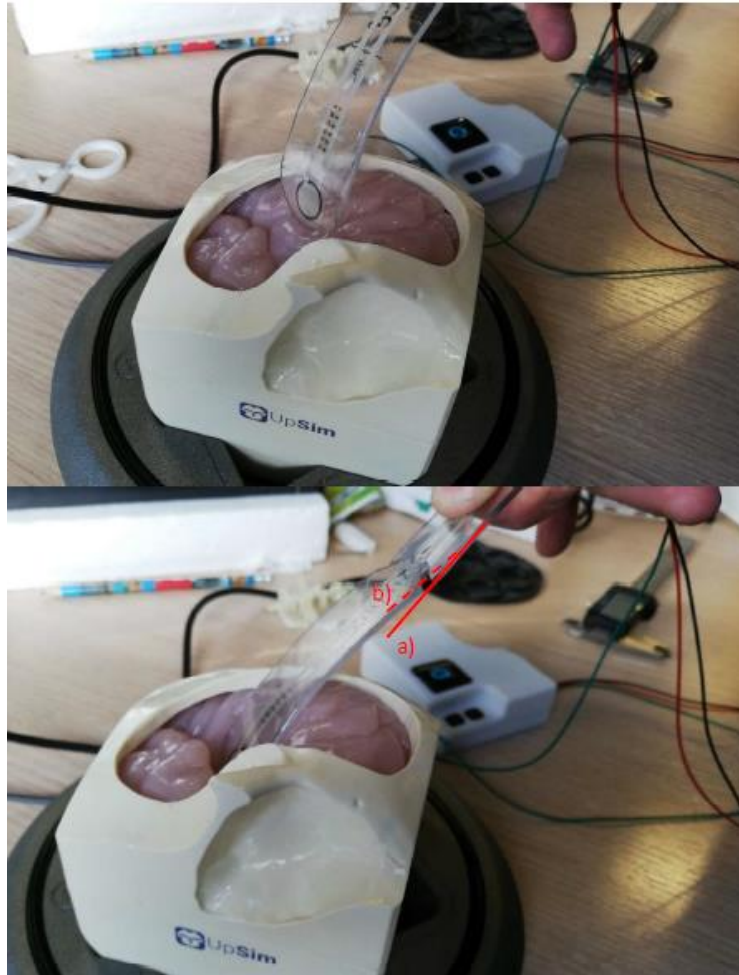
In order to obtain this result and this geometry, we proceeded experimentally starting from a sample of polycarbonate with a curvature similar to the reference one of a traditional spatula. The sample was cut manually following the profile of the spatula and subsequently the necessary notches were made to create the flap. The depth of the notches was evaluated from time to time using a digital scale with a resolution of one tenth of a gram so as to quickly understand the forces involved.



a) CAD model of the spatula with the greatest dimensions. b) First prototype of the spatula transparent.

Once a flap size of 7.88 mm was reached, the FlexiForce TekScan system and the UpSim simulator were used again to have a more faithful correspondence with the real pressure values exerted by the spatula and the relative sensation returned.

The system was composed as in figure below and the test consisted in carrying out the greatest possible retraction until the sensation of breaking the spatula was perceived, which consisted in passing the line a with respect to the line b.

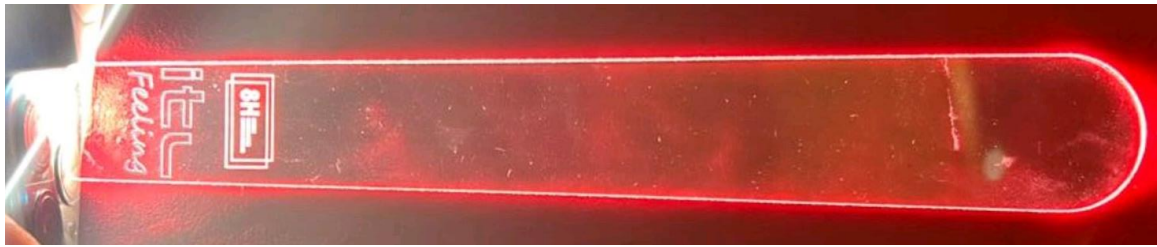


Test on preclinical model made by Upsurgeon s.r.l.

Initially, the detected pressure easily reached 70mmHg, an excessive value that led us to reduce the section to obtain the 7mm previously presented. In fact, with this geometry the tests carried out in the same way led to the maintenance of the pressure below the critical value of 50mmHg.

Once this spatula was proposed to the neurosurgeon, the effectiveness of the sensation of exceeding the pressure value was confirmed, however, a limitation of the spatula emerged, namely the difficulty of adapting it quickly according to needs as is currently possible with steel spatulas. In order to overcome this limit, yield points were carried out in the area in contact with the parenchyma, so as to obtain areas that can be easily deformed while maintaining the given shape.

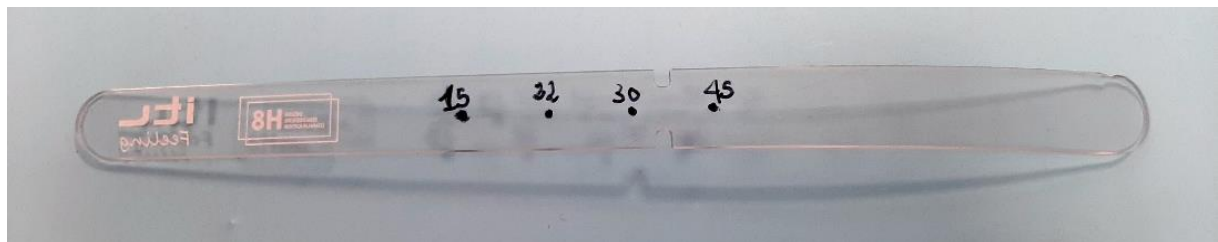
To further improve the versatility of the spatula, a LED was inserted that could illuminate the tip of the spatula.



Illumination of the spatula

This was possible thanks to the particular optical properties of the polycarbonate which behaves like an optical fibre, i.e., the light does not come out of the spatula profile, but is reflected and then transported from the point of contact with the light source to the tip of the spatula.

We have also designed the spatula considering different corresponding grip points at different pressure levels. Thanks to this ergonomic shrewdness it is possible to choose the retraction pressure to be exerted and, at the same time, to safely retract the brain being aware of the force being exerted on the parenchyma.



Handle of the spatula at different pressures of force

Finally, a cannula was inserted on the side of the spatula so that it can be connected to an aspiration system so as to allow the deliquoration operations necessary to remove the organic fluids, allowing to proceed with the surgical operation.

9.2 CHAMBER

As presented in the previously described studies a strong criticality of traditional spatulas is the concentration of load that is created along the edges, increasing the possibility and severity of lesions to the brain parenchyma. This problem recurs in the same way in our transparent spatula, it was therefore necessary to find a solution.

The solution consists in the use of the device shown in figure below, the chamber, consisting of two identical halves that can be opened so as to perform a softer retraction and with a curvature such as to reduce the effects of pressure concentration.



First prototype of the chamber inserted in the cadaveric sample.

In addition to reducing the pressures exerted on the parenchyma, the chamber also creates a surgical corridor that allows you to operate, with a robotic arm, without the risk of accidental impacts that would seriously damage healthy tissue.

The halves that make up the chamber were made of PLA through 3D printing, as can be seen from figure below the geometry presents variations in sections, grooves, which allow to reduce the stiffness so as to allow deformation and obtaining the cylindrical geometry of the chamber.



Half that makes up the camera, on the right for the 22mm camera and on the left for the 40mm one

For surgical needs, the chamber had to reach a proximal dimension, i.e. in the area closest to the lesion, final of about 20mm x 10mm, starting from this the size of the half was defined, which was identified as being 44mm wide and 70mm deep.

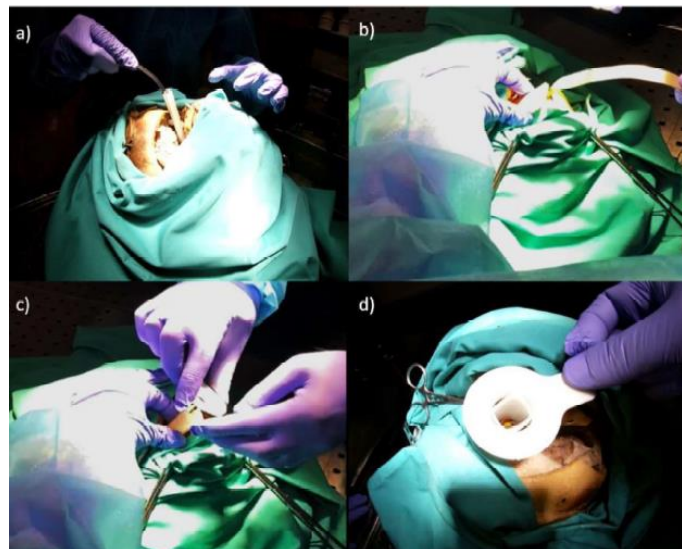
The two halves of the chamber were then joined by welding the specially created tabs.

To allow the closure of the chamber to be maintained and any movement, an accessory has been created (Figure below) which, once inserted, prevents the chamber from opening. It also has a projection made in order to be able to insert it into the reference instrument holder arm, so as to avoid the neurosurgeon having to constantly keep one hand occupied.



Lid to lock the chamber and attach it to the instrument arm.

The chamber was tested by the neurosurgeon on the fixed specimen and four stages leading to its complete unfolding were identified.



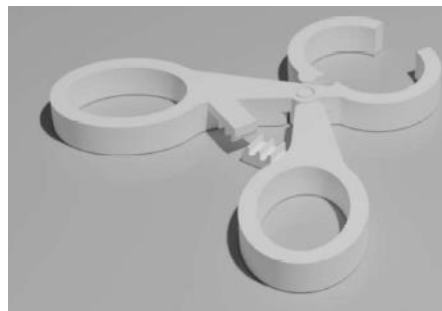
Phases of Chamber positioning: a) insertion of the chamber in the area of interest through the use of a retractor. b) Removing the retractor and holding the chamber in place. c) Manual opening of the chamber up to the desired size. d) Insertion of the lid and possible locking.

Following the tests carried out on the cadaveric sample and the comparison with the surgeon, it was decided to modify and improve some aspects of the chamber.

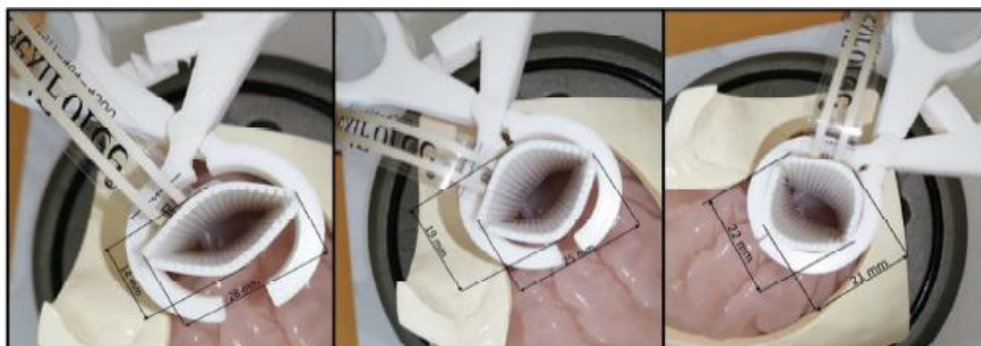
First of all, the height of the chamber has been reduced from 70mm to 50mm since it protruded excessively from the intervention area, however this may depend on the specific case of the lesion to be treated, so it is obviously possible to create chambers with different depths.

A further change inherent in the geometry was to eliminate the circular part at the apex of the chamber making it flat, this to ensure that the end part remained more in line with the profile of the chamber. This geometric change also resulted from a different operating methodology. In fact, as mentioned, the original idea was to use the chamber with the spatula to retract the parenchyma and subsequently remove the spatula, this procedure was more complex than expected and for this reason it was decided to retract the tissue with the spatula alone. and then enter the chamber.

In order to improve the control of the opening phase of the chamber, a klemmer type pincer was designed that could facilitate the management of the chamber, avoiding to cover the visual field with the hands and providing three closing clicks that lead to a retraction pressure performed by the chamber as constant as possible.



Klemmer gripper model for the smallest chamber.



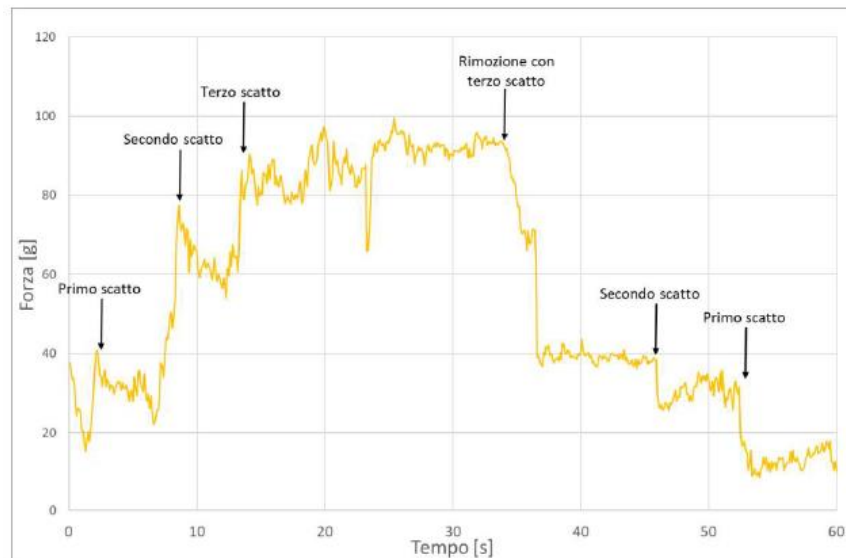
Measurements of the chamber opening respectively first (14mmx28mm), second (19mmx25mm) and third (22mmx21mm) snap.

Similarly to what was done with the transparent retractor, thanks to the use of the forceps and the FlexiForce measurement system it was possible to calibrate and verify that the chamber did not exceed the critical retraction pressure value.

To do this, the sensor was positioned in two different positions: central with respect to the axis of one half that makes up the chamber and laterally.

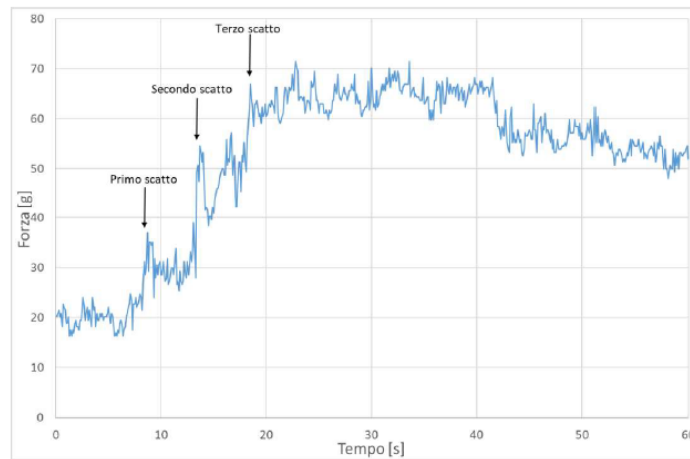
The decision to investigate the two different positions is derived from two main considerations, first of all assessing whether there were differences in pressure as the area of the chamber varies and, secondly, because the opening of the chamber causes the sensor to deform in a way that which is not designed and this generates a false reading more or less accentuated according to the level of curvature reached by the sensor.

The graphs below deriving from the tests are shown below; both graphs show the first, second and third snapshots that identify the closing phases of the klemmer.



Retraction forces deriving from the opening of the chamber with the central sensor. You notice how even once extracted from the simulator, the sensor produces readings.

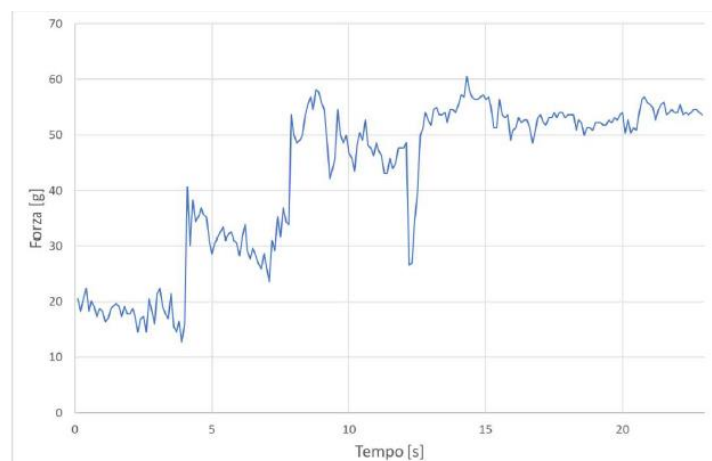
In the first graph, referring to the central sensor, it can be seen that the pressure values detected are significantly higher than those of the second graph. This difference is attributable only to the greater deformation to which the sensor is subjected which leads to obtaining false readings. Once the chamber has been removed from the simulator, the force reading shows a significant drop, but it does not reach zero as it should and settles on the value of about 40g. This allows us to evaluate the net value as a delta between the reading with the chamber inserted and the reading just described at about 50g, a value which in mmHg is substantially identical.



Retraction forces deriving from the opening of the chamber with the lateral sensor allowing to have fewer false readings.

The phenomenon and reasoning just described also apply to the first and second shot and to a lesser extent in the configuration with the sensor positioned laterally where only the third shot has a false reading, however limited to 10g.

The following graph shows the test performed in the graph aforementioned, but with the net data so as to have a more accurate perception of the forces really at play during the opening of the chamber. The data presented in the graph have been made considering the values of the different clicks in the linear and non-passage areas for ease of identifying a certain deformation value of the sensor that would allow to remove the staggered reading component due to this deformation. For this reason, the graph starts from instant 0 with the chamber already open at the first click of the klemmer and therefore only two jumps and not three as happened in the graphs previously shown. This approximation of presentation was also necessary due to the reduced time available since, remember, the maximum data recording time is 60 seconds.



Representation of the net values of the test shown in figure-2

The table below shows the net force values of the tests carried out with the sensor centred and on the side. Of the lateral sensor the data present refers only to the third click since the first two did not present false readings and the data of our interest is the maximum pressure exerted.

	Media camera aperta [g]	Dev st
<i>Scatto1</i>	18,1062432	2,150069
<i>Scatto2</i>	31,5751874	3,589287
<i>Scatto3</i>	51,71084033	4,805812
<i>Sensore laterale</i>	46,85110501	11,32185

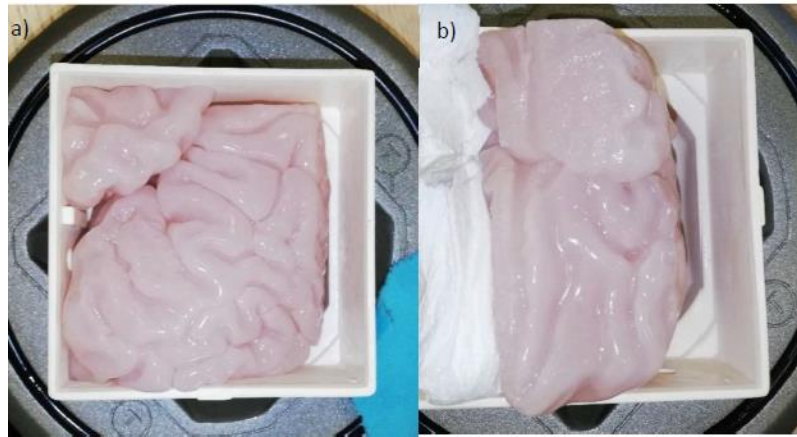
Values of retraction force referred to the clicks of the gripper.

From the data presented in the table it emerges that the average values of the central snap sensor3 and of the lateral sensor are statistically comparable and around the critical pressure values, making the use of the chamber safe during a neurosurgical operation.

A further larger chamber was then created that would allow to reach greater retractions and generate a wider corridor, so as to allow adaptation to the different anatomy possibilities of the patient and the lesion. The largest chamber has been designed to provide double the space compared to the first, so the width of one half is 63mm, so as to reach, once closed, an internal diameter of 40mm and an external diameter of about 42mm.

Given the greater retraction, it is easy to understand that in the case of use entirely similar to that of the 20mm chamber, greater retraction pressures would have been reached. In order to investigate the pressure levels involved, some changes were made to the simulator, since the original configuration did not have enough space to ensure the insertion and opening of the chamber.

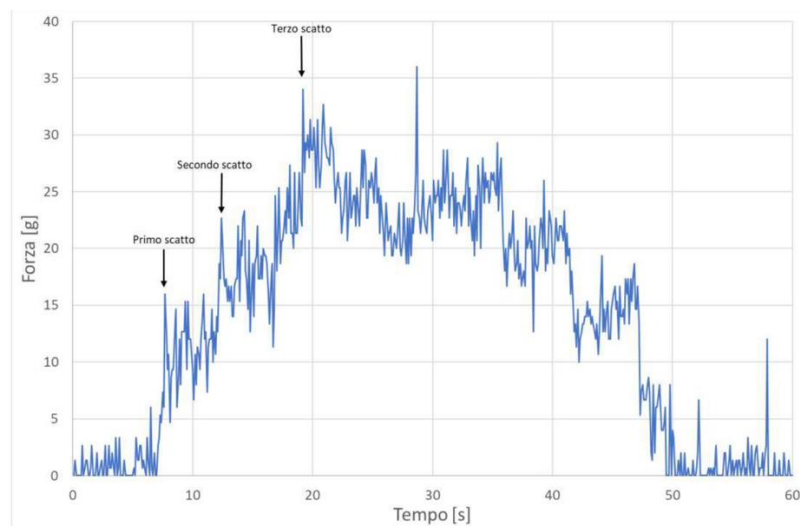
The base was removed and the silicone part, which simulated the cortical area, was inserted directly into the lower area of the box. As shown in Figure below two positions of the silicone model were used to ensure different distances from the rigid wall, so as to simulate a variability of spaces between the parenchyma and the cranial bone.



a) Test setup with very little space to investigate maximum force values
 b) Configuration with a skull parenchyma space of about 15mm, more realistic situation.

The first tests performed were those relating to the most critical condition, that is with the brain parenchyma. The sensor was positioned in two different positions: proximal, i.e. the closest to the hypothetical lesion and distal farthest from the lesion, in particular as high as possible considering the size of the forceps.

The graph in figure below shows the false sensor readings when the different shots are taken, these readings are obviously without load.

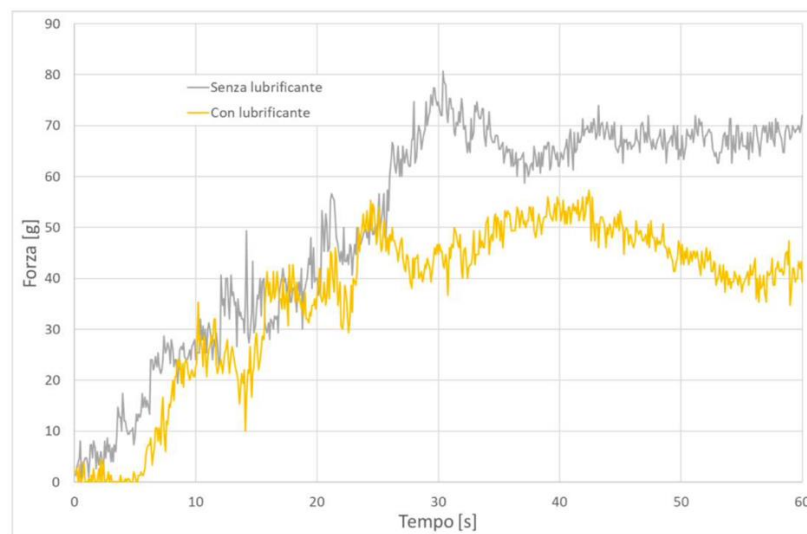


Values of false readings deriving from the deformation of the sensor when opening the chamber.

As you can see, the readings turn out to be about 25g in the case of the third shot, they are therefore lower than in the case of the sensor positioned centrally in the small chamber, but higher with the side sensor. However, it must be specified that these values cannot be subtracted directly from the values read during retractions since the deformation applied to the sensor during retraction is lower

than in the case of the graph because the proximal part of the chamber deforms less due to the presence of the tissue.

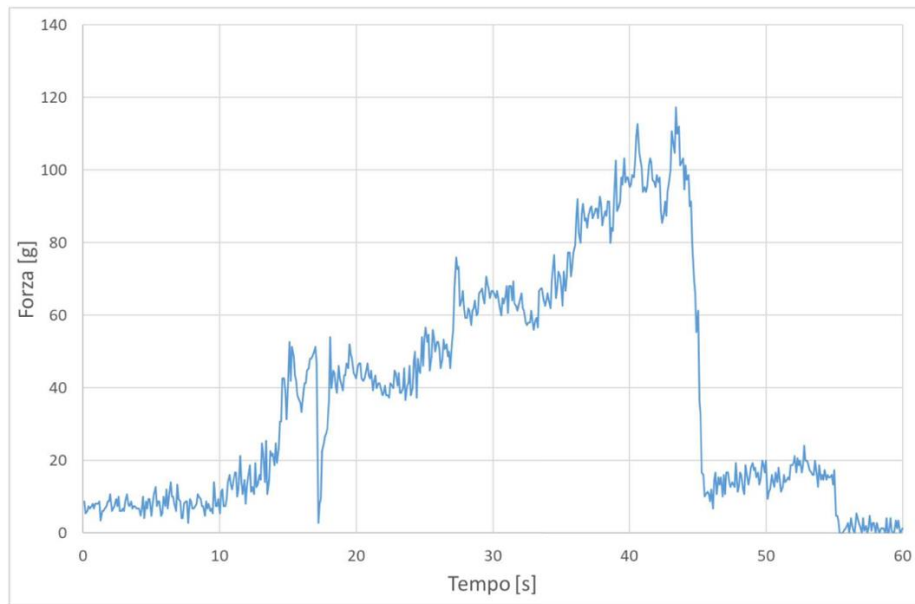
The graph below shows two tests performed with the proximal sensor as in figures aforementioned a) with the simulator positioned, the first was performed after some preliminary tests and without lubrication, in the second a lubrication had just been performed. The lubricant considerably reduces the pressure values detected; from the experience gained during the study, we believe that these are the most reliable values in the case of application on human brain parenchyma.



Comparison between two retraction tests performed with and without lubrication of the simulator, it is noted that the force values with lubrication are significantly lower.

The values reached in the lubricated case are lower than the critical reference value so as to make this chamber theoretically always applicable even with considerable retractions and starting from small spaces. This reasoning has, however, been debunked by tests carried out with the sensor positioned distally, since it is in proximity to the clamp where the greatest retraction and theoretically the highest-pressure values are obtained.

The various tests have in fact confirmed this assumption as shown by the graph below we can see how the pressure reaches high values, in particular peak values around 100g are reached. This makes it impossible to apply the chamber since these values would cause permanent damage to the tissue and therefore to the patient.

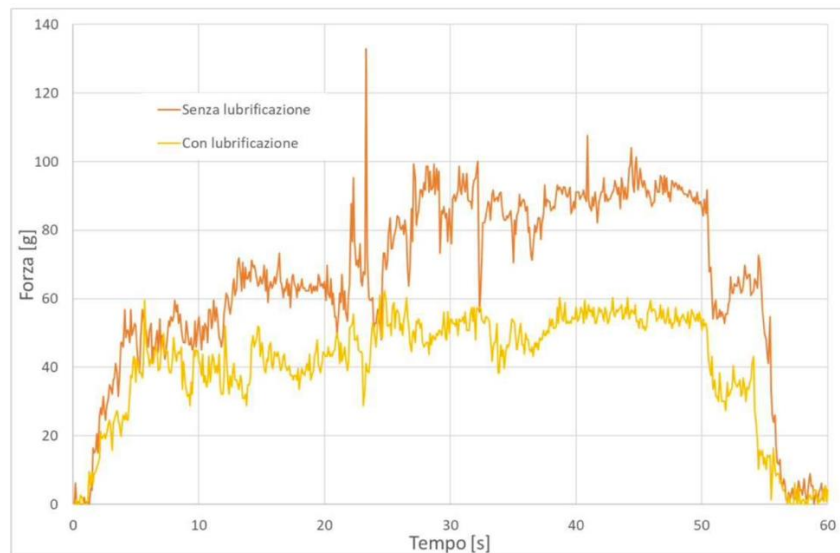


Force values with the distal sensor. We see how the force largely exceeds the threshold values making this device unsafe.

Tests were then performed with the simulator in configuration b of figure aforementioned, which allowed to simulate a situation of previous retraction or anatomy of the patient such as to guarantee a space between the skull and the parenchyma of about 15-20mm.

Also in this case the tests were carried out with the distal and proximal sensor, in any case the sensor was positioned slightly less in depth even in the proximal case since from the tests just presented it is evident that the higher pressure is in the distal area.

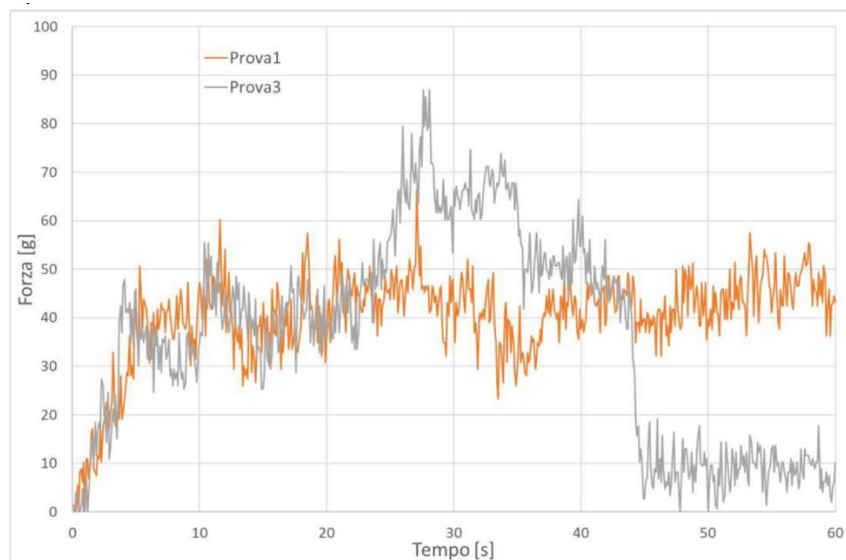
The following graph shows the data obtained in the proximal case, in particular the difference in retraction pressure obtained according to the lubrication used on the simulator is highlighted. Once again, we see how the presence of the lubricant greatly decreases the retraction forces, bringing the chamber to acceptable levels, especially considering the false readings given by the deformation of the sensor.



Comparison between retraction force values with and without prior lubrication. The significant reduction in the presence of lubrication is confirmed

The tests were then performed with the distal sensor, trying to position it as close as possible to the forceps where there is the greatest retraction.

Figure below shows the graphs of two tests carried out in this way; all the tests were performed after lubrication for the reasons given above.

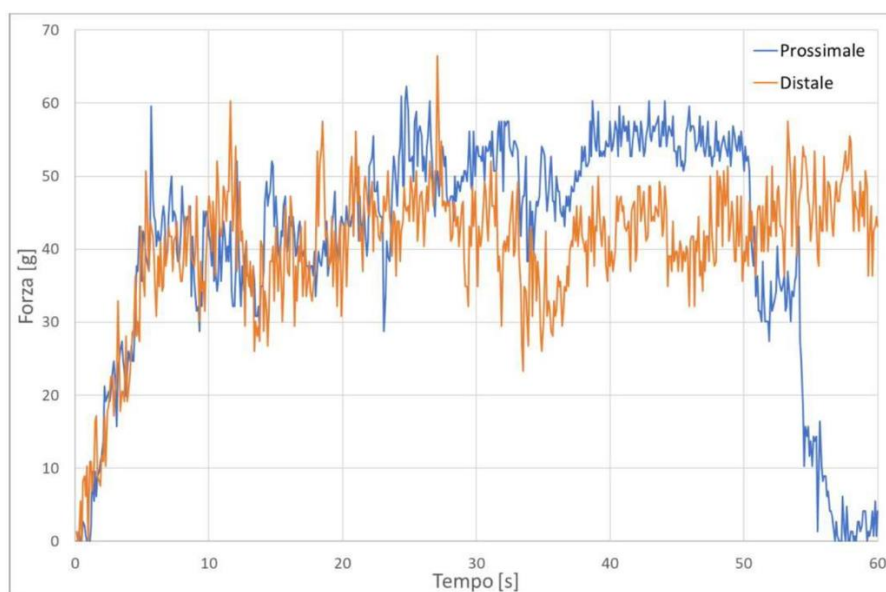


Two chamber opening tests compared. The peak present in test 3 derives from inappropriate handling

From the graph it can be seen that in test 1 the critical value of 50g was kept constantly. In test 3 the peak of force is due to the attempt to insert even deeper into the chamber at maximum opening, to have a view of possible increases in force, this is not the case, in fact once the thrust is stopped the force returns to acceptable values.

Following figure shows the comparison graph between two tests in distal and proximal configuration, it is easy to see how there is no substantial difference between the two tests, in which the strength values are kept close to 50g, which should be purged of the values of false reading, not easily identifiable, but which are certainly of the order of at least 10g.

From the tests performed we can therefore state that the chamber of this size can guarantee a safe retraction only when there is sufficient initial space, identified of at least 15mm. In operative practice this dimension can be evaluated by using the smallest camera, in fact the first snapshot reaches 14mm, while the second one 19mm, by opening the camera and evaluating when the contact with the cerebral parenchyma occurs, it is possible to have a verification of maximum of the initial distance.

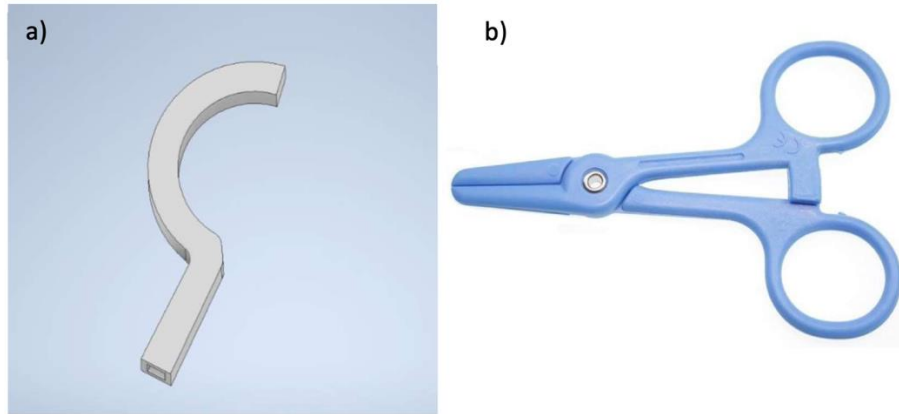


Comparison of the retraction force values with the sensor in the proximal and distal position, no significant differences are found

Extension for Klemmer pliers

As an alternative to the pliers we designed, an attempt was made to create a multipurpose tool that could adapt to the various diameters of the chamber.

To do this, a klemmer pliers of the type shown in figure 5.19 have been identified as the basis. It was machined manually by removing chips in the end in order to provide sufficient space between the two allowing the insertion of extensions designed by us.



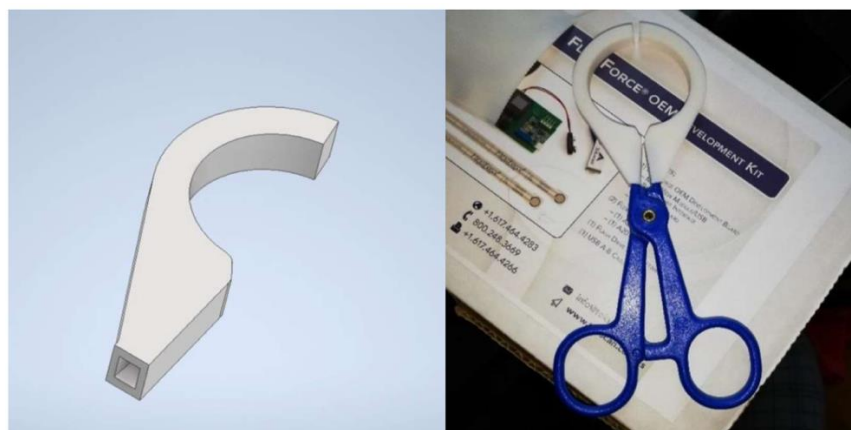
a) CAD model of the extension for the smallest chamber b) Klemmer pliers used as a base for the extensions

As mentioned, the idea of the extensions was that they could be used to create a suitable tool for closing and managing chambers of different sizes without having to have several pliers, but a single adaptable klemmer.

The first version of the extension was found to be ineffective, in fact it was not sufficiently rigid to be able to obtain the complete closure of the chamber. Furthermore, once inserted on the klemmer, cracks were caused on the innermost flap due to the limited thickness.

In order to make the extension functional, the geometry was modified as in figure 5.20, in particular the thickness of the breaking area was brought from 0.5 mm to 1mm and a rib was created that would provide sufficient rigidity to the extension to avoid its deformation when closing.

Despite these precautions, it was not possible to use this tool since the improvements have increased the stiffness of the extension, but that of the ends of the klemmer was insufficient, probably due to the excessive loss of section due to the machining. Although it could be useful as a tool, it was therefore abandoned given the impossibility of increasing the intrinsic stiffness of the available klemmer.



a) Final CAD model of the extension. b) Extensions mounted on the klemmer caliper for the 40mm chamber

10. ANIMAL STUDY PHASE

Having carried out the preclinical study phase allowed us to comply with the criteria of phase 1 of research development in surgery. This step was also fundamental to prepare us for the next one which sees the experimentation of the device on animals.

The completion of this last phase will then allow us to carry out the subsequent clinical study phase in the operating room on the patient. From an accurate analysis of the literature, as well as from a detailed anatomical study, we have evaluated to perform animal experimentation using the pig genus. The need to use the pig as an animal stem from its resemblance to the human brain compared to other species. A suine of about two quintals has a brain with a weight of about 110 grams.

Experimentation on animals involves two phases: a first in which the procedure is carried out on a dead animal and the second on a live animal. In order to optimize the method to reduce the suffering imposed on the animal during the execution of the procedures, the tests will be carried out first on dead animals.

In consideration of the guidelines on animal testing, our procedure is classified as "not serious" since the animal also performs the non-awakening procedure so there is no suffering for the animal.

The animal falls asleep during the surgical procedure and therefore there is no suffering. The only possible suffering could be that of pain during the surgical procedure but, in order to remedy this, specific pain relievers are administered.

10.1 MINISTRY OF HEALTH APPROVAL: legislative decree March 4th, 2014, n. 26

Many retractor instruments dedicated to skull base surgery have been described, but their application has been limited by physical characteristics and inefficient control over brain retraction. There are currently no tools that include several advantageous features including brain pressure measurement. Furthermore, the preliminary studies carried out, both on a preclinical model and on samples, have documented how the surgeon's movement can vary when he is aware of the level of pressure he is exerting on the parenchyma.

We believe that our new spatula can bring significant benefits to the surgeon and to the success of the surgery by ensuring a better and safer post-operative outcome for the patient.

Furthermore, we investigated the dynamic mechanical characterization of brain tissue, and intriguing features emerged that had never been analysed before. These data could prove useful for identifying mathematical models that analyse brain tissue response under arbitrary load conditions to improve computational systems for predicting the mechanical behaviour of the human brain under health and disease conditions.

Effects on human and / or animal public health

The possibility of using our new instrument experimentally also on animals, as well as already carried out on a corpse and preclinical model, will allow us to move on to the decisive step using the device in the operating room on the human brain.

The study phase on animals is essential before proceeding to humans: the analysis of the tests we will carry out will allow us to collect valuable information about brain behaviour when subjected to a retraction force.

These data, combined with an accurate mechanical, dynamic and histological mathematical analysis, will guarantee us to obtain specific knowledge on the brain that could prove very useful in both healthy and sick patients.

The possibility of carrying out a controlled brain retraction, i.e., perfected thanks to the specific force sensors of the new device, could significantly reduce the risk of surgical complications from cerebral retraction.

All this would have a great positive impact on the patients' postoperative surgical outcome; in particular, it is often about cancer patients for whom the reduction of complications is essential for a better survival.

Possible impact in the economic-industrial sector

The possibility of carrying out the experimental tests of our new surgical device, even on animals, is an important step also for the purposes of a future patent for the subsequent marketing of the aforementioned.

Possible repercussions in the field of training

The results will be published in international journals, so the data will be available to the scientific community to deepen and implement information on the topic. The use of the new device, once its best functionality has been documented, could also be used in the neurosurgical learning curve in order to train young neurosurgeons.

Declarations referring to article 13, paragraph 2 of the decree

- The need to use the pig as an animal stem from its resemblance to the human brain compared to other species. The experimental study on animals is necessary for the subsequent passage to the clinic or to the operating room on the patient.
- A minimum number of animals will be used to meet the study objectives.
- In order to optimize the method to reduce the suffering imposed on the animal during the execution of the procedures, the tests will be carried out first on dead animals

- In consideration of the experimentation that we will perform, we do not consider the procedure classified as "serious" since the animal will also perform the non-awakening procedure so there will be no suffering for the animal. The animal will be asleep during the surgical procedure and therefore there will be no suffering. The only possible suffering could be that of pain during the surgical procedure but, in order to remedy this, specific pain relievers will be administered.

10.2 METHODOLOGY AND TECHNIQUE OF THE EXPERIMENT

With a meticulous systematic review of the literature, we first studied brain retraction by analysing the forces involved, the pathophysiological mechanisms and possible complications on the patient. The geometry of the spatulas currently used produces a high concentration of pressure along the edges, the opacity of the retractor does not allow you to have a constant view of the retracted fabric and, finally, there is no way to know the value of the pressure that is applied during retraction. First of all, it was necessary to simulate the use of a spatula, a tool usually used in neurosurgery, to analyse the effects of retraction on the brain parenchyma. We then performed the first experimental tests of the spatula on a 3d anatomical model testing the reaction of the brain parenchyma: different surgical approaches were simulated by calculating the values of the forces involved for each of these. First of all, tests were performed with the surgical spatula currently used in neurosurgery: the structural analyses performed confirmed that a modification of its geometry is necessary to reduce local pressures during retraction and avoid damage to the brain parenchyma. Currently, in fact, one of the complications of neurosurgical interventions is the damage caused by spatulation due to excessive cerebral retraction.

Consequently, it was essential to identify a suitable measuring instrument that would allow to detect the back pressures. It was then placed on traditional retractors so that it could provide the surgeon with real-time retraction pressure values during the operation. Subsequently a new spatula was designed, no longer in metal but in polycarbonate so as to be transparent and allow you to see the retracted fabric and evaluate its state over time.

Finally, an instrument was created that could combine the versatility of the spatulas with the reduced pressures of the tubular retractors, this instrument consists of a chamber that can be inserted closed and subsequently opened, using a special pliers, of the Klemmer surgical type, creating a safe corridor. for the insertion of the endoscope for use in transcranial and ventricular surgery. Thanks to the sensor system it was possible to ensure that both the spatula and the chamber did not exceed the critical pressure values during their use, while obtaining the necessary retraction to visualize the target. This prototyped spatula, undergoing further development and in vivo study, allows to study

the effects of its geometry on the brain and the pressure values involved, as well as all the forces involved during a neurosurgical operation.

The tests carried out on non-in vivo animals have made it possible to fine-tune and perfect the surgical technique and experimental tests in an optimal manner.

In vivo tests will be performed in a single intraoperative phase on previously anesthetized three pigs.

Sample selection criteria

The inclusion criteria will focus only on the analysis of the skull and brain tissue which must be free of anomalies and / or previous damage. There will be no sample subdivision into groups.

Statistical considerations

Sample size was assessed based on the literature and the availability of statistical units. Measurements will be displayed as mean $\pm$ standard error. Statistical analyses will be performed using mixed models and statistical methods for small samples. Statistical significance will be considered for any P value less than or equal to 0.05. All analyses were performed using this statistical software R. (<https://www.r-project.org/> Applied Asymptotics: Case Studies in Small-Sample Statistics, Cambridge University Press, A. R. Brazzale, A. C. Davison, N. Reid (2007)).

Risks for the operator

No risk. In any case, the precautions normally applied in laboratory practice are used as well as the safety measures required by law and the suitable precautions normally used in the operating room.

Adverse effects and measures to reduce, avoid and mitigate any form of suffering for the animal from birth to death

The animal will be put to sleep with anaesthetic technique by administering suitable drugs and the non-awakening procedure will be carried out. Therefore, there will be no negative effect on the animal.

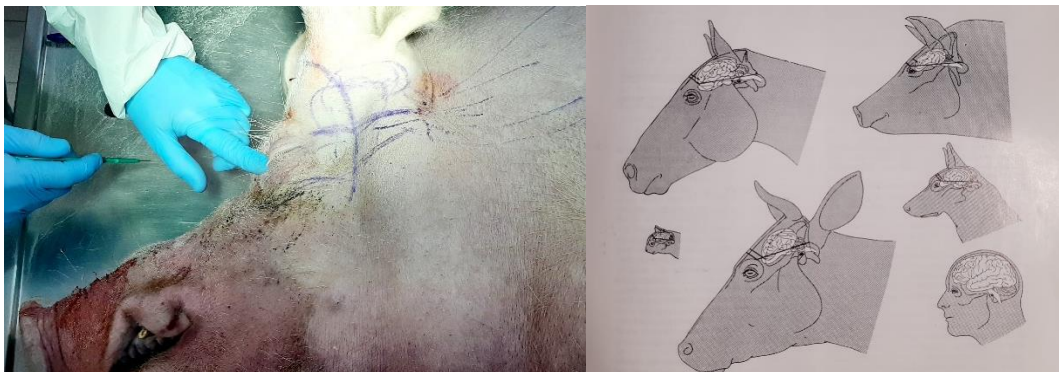
10.3 DECEASED SUINE PHASE

Surgical step 1



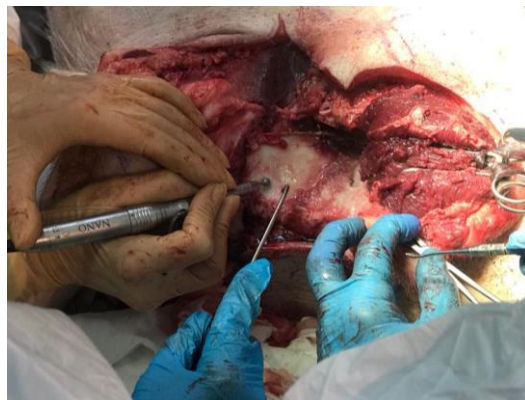
Positioning on the operating table

Surgical step 2



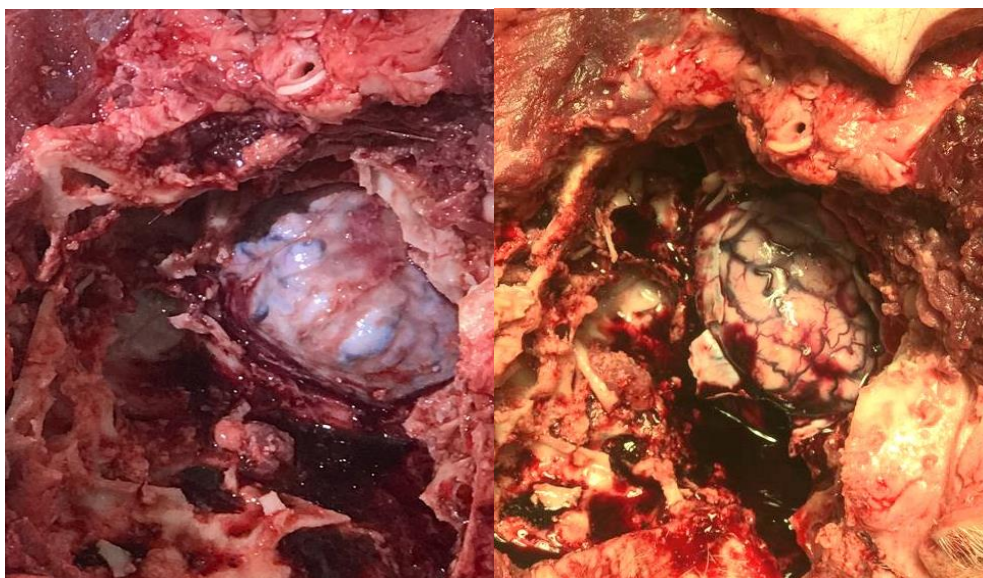
Tracing of skin landmarks

Surgical step 3



Craniotomy

Surgical step 4



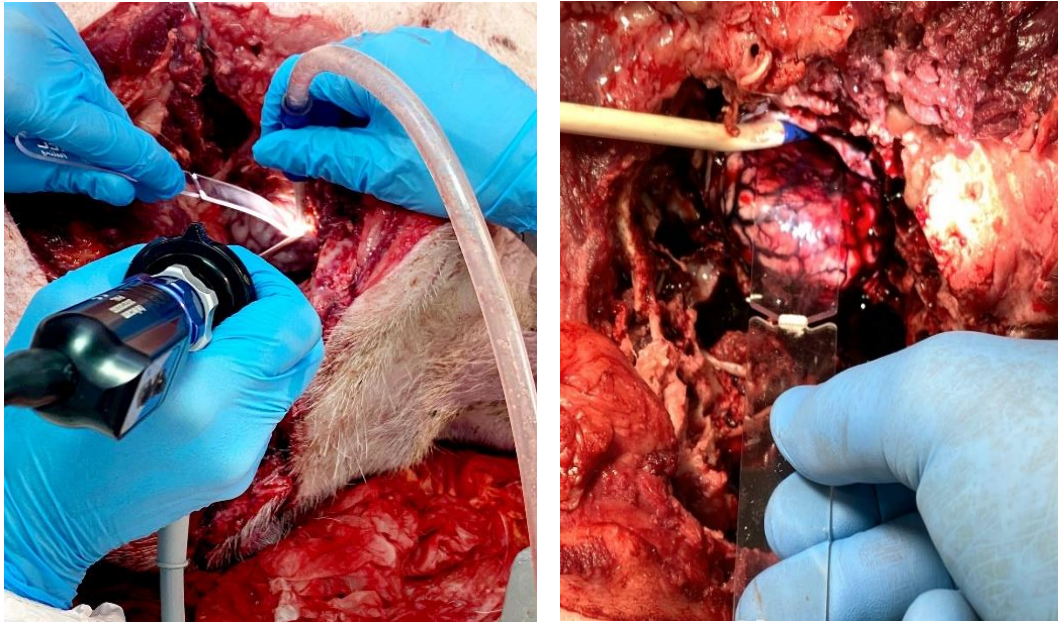
Visualization of the dura mater and opening of the same

Surgical step 5



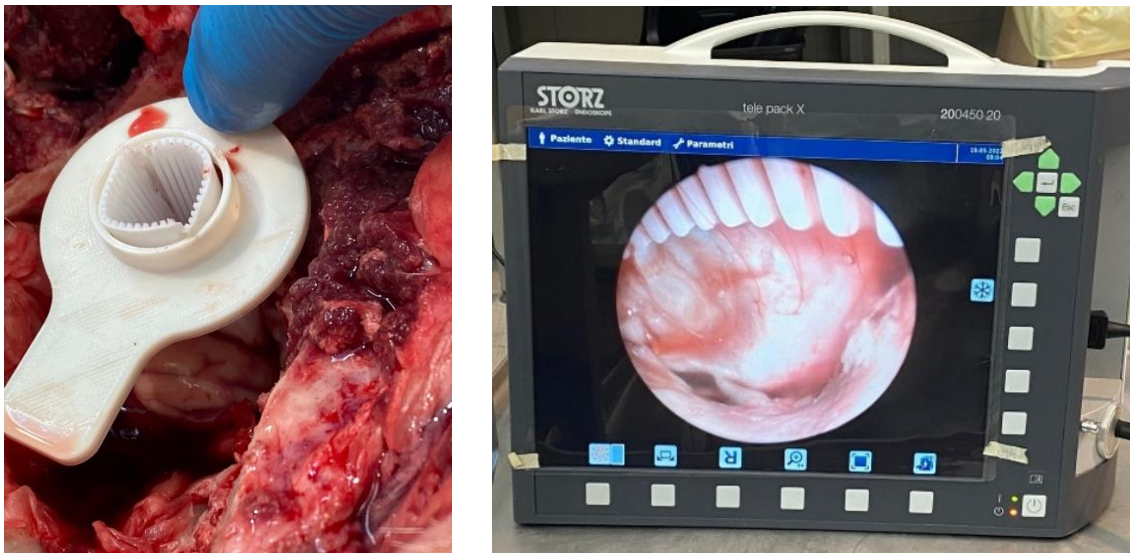
Brain retraction tests using monitoring pressure system

Surgical step 6



Brain retraction test with our new spatula device and use of the endoscope

Surgical step 7

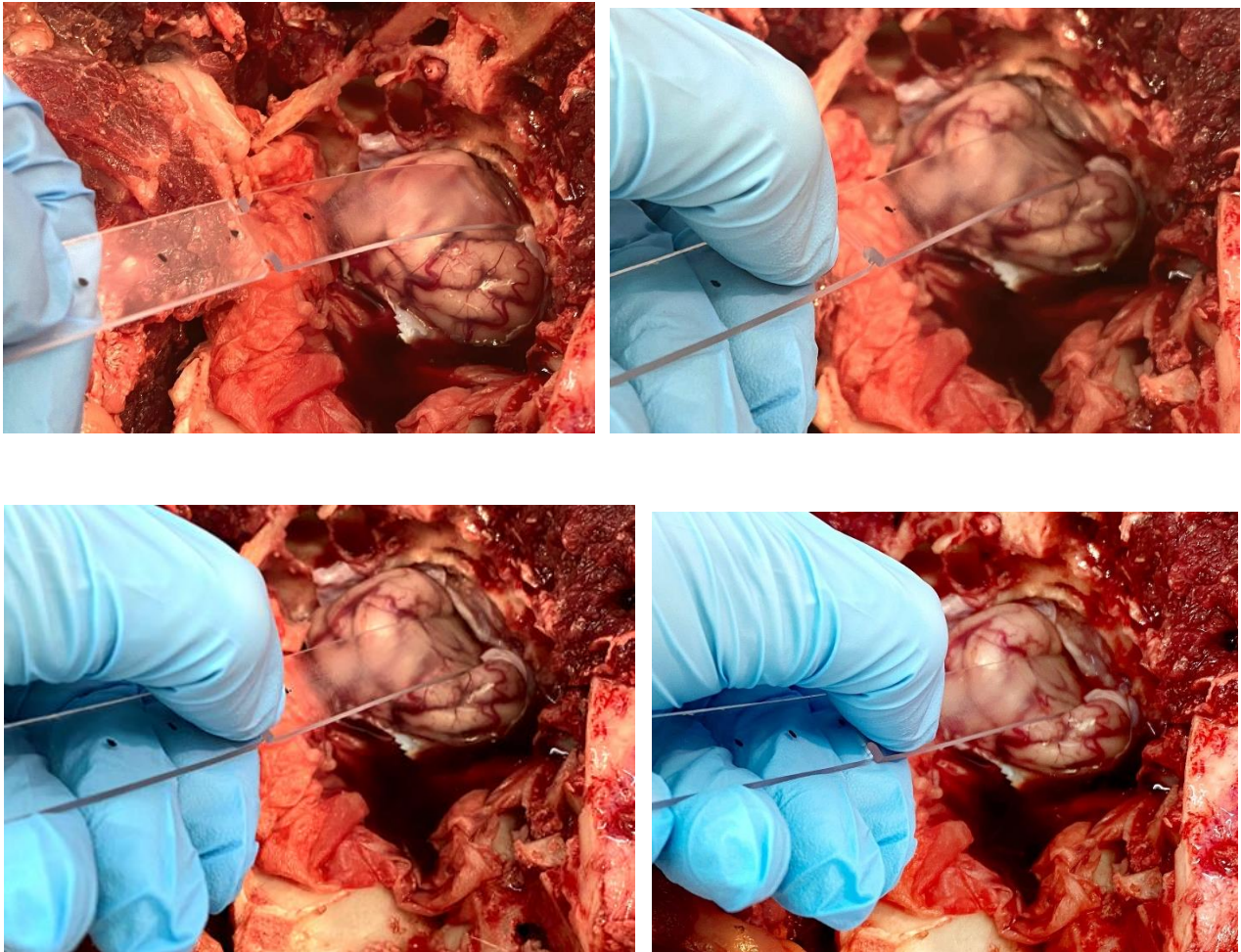


Brain retraction test with our new chamber device and use of the endoscope: visualization of the optic nerve.

Microscopic histological analysis

We remove brain parenchyma samples and initially divided them into two groups: brain subjected to spatula retraction and brain not retracted.

Subsequently we carried out some samples of brain parenchyma subjected to different retraction pressures: 15, 22, 30, 45mmHg.



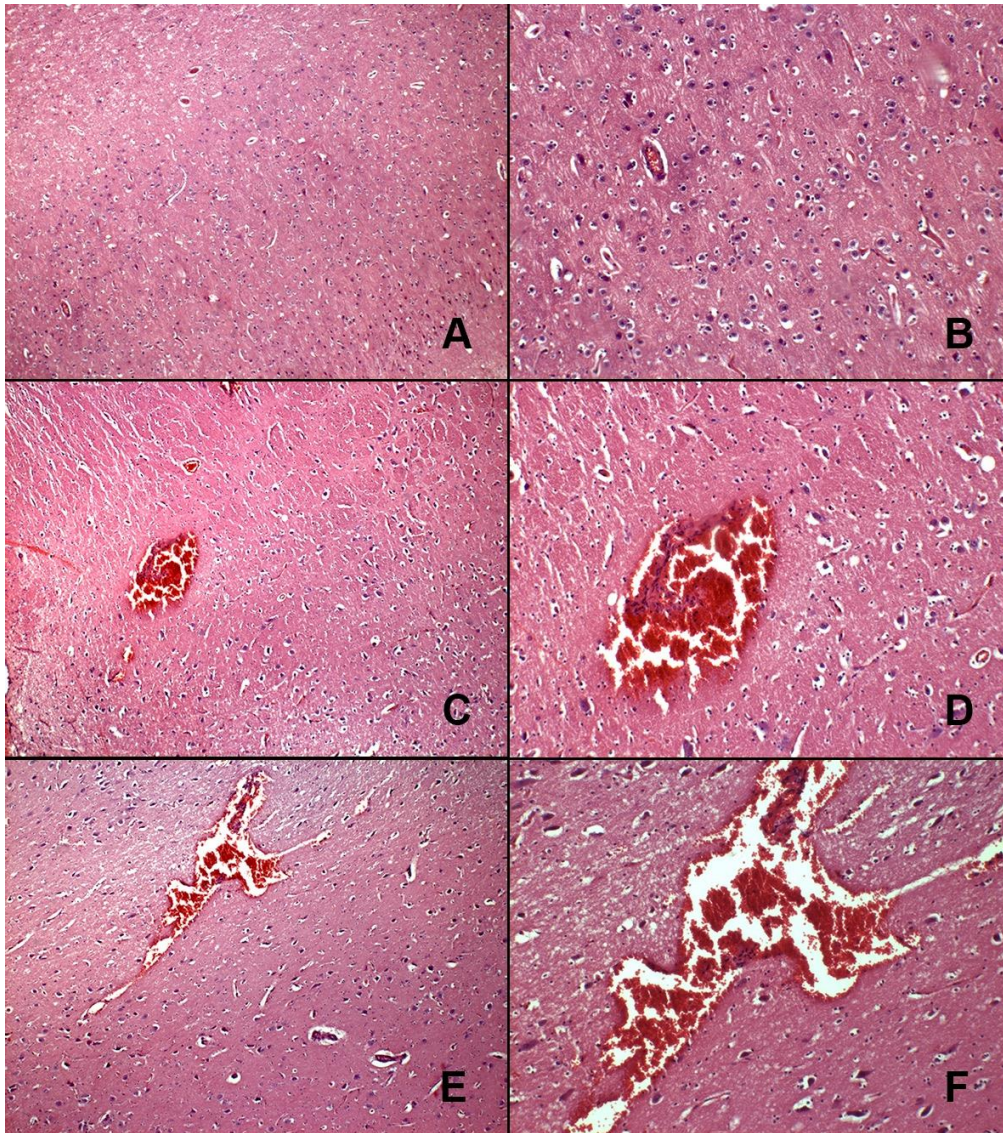
Handle of the spatula at different pressures of force: 15, 22, 30, 45mmHg

On these samples special staining with haematoxylin and eosin was performed to investigate the tissue alterations of the parenchyma subjected to retraction compared to that not subjected to pressure.

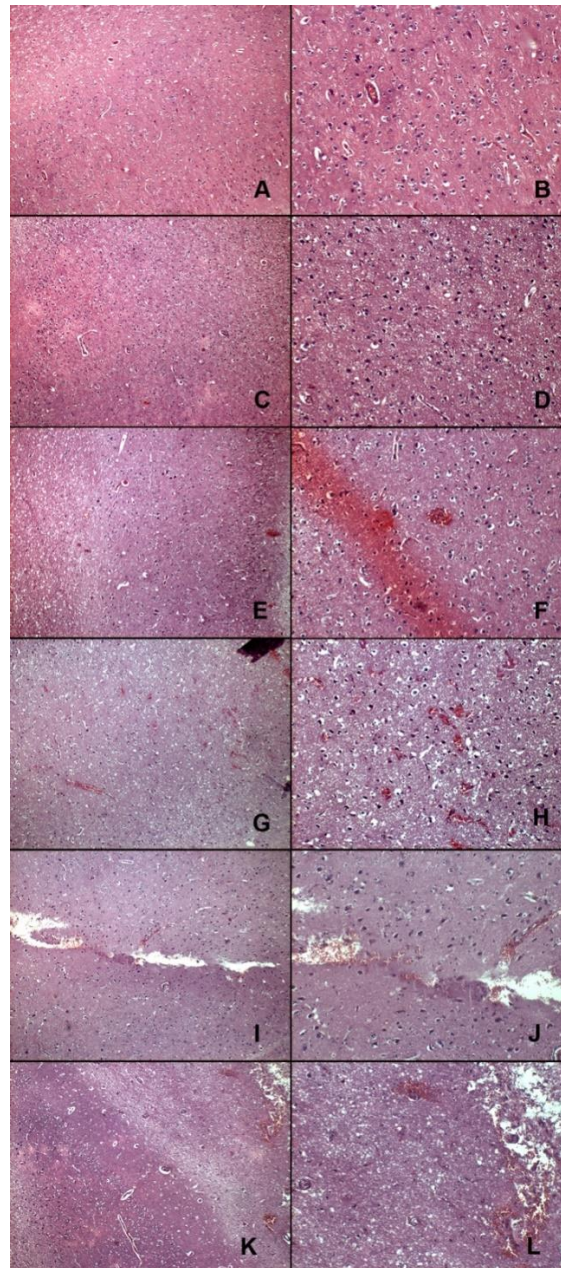
Materials and methods

Brain samples were processed for microscopic morphological evaluations. They were fixed in a 10% neutral buffered formalin solution and embedded in paraffin using automatic tissue processor (Donatello Series 2, Diapath BG, Italy). 5- μ m-thick sections were cut by microtome (Semi-automatic rotary microtome Galileo, Diapath, BG, Italy) and collected on poly-L-lysine coated glass slides. Sections were deparaffinized in xylene, rehydrated in descending alcohol concentrations, and stained

with Haematoxylin-Eosin and Masson-Goldner staining by using automatic stainer (Giotto, Diapath, BG, Italy). The microscopic slides were then observed under a light microscope at 4X and 10X (Olympus, Milan, IT), connected to a computer equipped with image analysis software (Image-Pro Premier 9.1, Immagini e Computer, Milan, Italy). Both macroscopic and microscopic evaluations were performed by two operators unaware of the processed samples.



A-B) Control – without retraction at a final magnification of X40 (A) and X100 (B). **C-D) E-F)** Treated (PIG 1 normal Spatula) - Microbleeds associated with a spongy tissue destruction after brain retraction at a final magnification of X40 (C-E) and X100 (D-F). Hematoxylin–Eosin staining.



A-B) Control – without retraction at a final magnification of X40 (A) and X100 (B). **C-D)** Treated 1 (PIG 2 Spatula 15 mmHg) – No alterations were evident at a final magnification of X40 (C) and X100 (D). **E-F)** Treated 2 (PIG 2 Spatula 22.5 mmHg) Microbleeds associated with a spongy tissue destruction after brain retraction at a final magnification of X40 (E) and X100 (F). **G-H)** Treated 3 (PIG 2 Spatula 30 mmHg) Microbleeds associated with a spongy tissue destruction after brain retraction at a final magnification of X40 (G) and X100 (H). **I-J)** Treated 4 (PIG 2 Spatula 45 mmHg) Microbleeds associated with a spongy tissue destruction after brain retraction at a final magnification of X40 (I) and X100 (J). **K-L)** Treated 5 (PIG 2 Spatula intermittent retraction) Microbleeds associated with a spongy tissue destruction after brain retraction at a final magnification of X40 (K) and X100 (L). Hematoxylin–Eosin staining.

11. COMPLEMENTARY ACTIVITY: ROBOT ASSISTANT FOR BRAIN SURGERY

Another important topic in my research activity was the robotic assistant for brain surgery, in particular on the control systems that can be implemented, in particular, for transcranial endoscopic surgery. Most robotic arms currently in use in neurosurgery use a foot joystick which can often be uncomfortable for the neurosurgeon who already uses his foot to command the bipolar forceps. So, we tried to study a new control system that uses surgeon's head movements and we have started preliminary tests.

11.1 GENERAL WORKING PRINCIPLE

The solution proposed by Railab mainly consists of a software platform connected to a 2D camera and to a robotic manipulator (a DENSO VS-060 robotic arm, controlled by a DENSO RC8 robot controller). The Railab Control Platform offers tools and functionalities to process and convert commands from surgeons and doctors (natural gestures, like head movements) into instructions for robot motion.

In particular, it acquires information on the surgeon's intentions through a 2D camera and a Graphical User Interface (GUI). This information is elaborated and processed, and finally used to generate target positions for the robotic manipulator.

When computing the final trajectory for robot movements, the Railab Control Platform also takes into consideration “safe areas”, meaning a 3D volume that the robot is not allowed to enter or hit with any part of its body and kinematic chain.



Robotic system

11.2 ALGORITHM DESCRIPTION

The Railab Control Platform manages the interaction between the surgeon and the robotic manipulator analyzing and processing the images acquired by a 2D camera. In particular, it can estimate the head pose of the surgeon, and infer the meaning of the surgeon's request.

Surgeon commands are then converted into low-level motion commands for the robotic manipulator. The Railab Control Platform generates the trajectory from the current position of the robot to the target points, taking into account “safe areas” restrictions.

It is important to notice that the navigation space for the robotic manipulator is planned considering the whole body and structure of the robotic manipulator and of the endoscope, and not only the final point of the tool. In this way, the Railab Control Platform can guarantee that at any instant of time no contact with critical areas of the brain of the patient will happen, even in case of re-orientation of the endoscope far end inside the brain tunnel (e.g. the body of the endoscope does not hit the areas of the brain around the insertion tunnel).

The aforementioned operations are based on the assumption that robot “safe areas” have been beforehand imported and loaded into the Railab Control Platform, based on data coming from proper devices (e.g. Computer-Aided Surgery systems). This is a required step that must be performed by the surgeon, before every surgical operation (as it strictly depends on the type of surgery and on the patient).

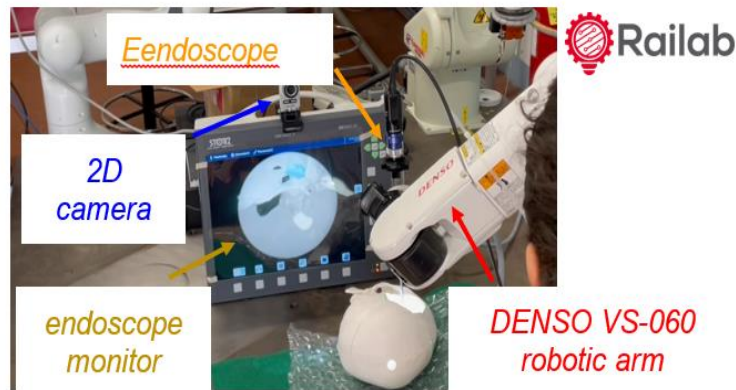
The operational flow of the Railab Control Platform can be summarized as follows:

1. 3D data are imported and loaded into the Railab Control Platform, and used to create “safe areas” for the robotic manipulator;
2. when starting the surgery on the patient, the surgeon activates the Railab Control Platform;
3. the Railab Control Platform infers intentions and commands of the surgeon based on the images acquired by the 2D camera;
4. based on the inferred intentions of the surgeon, the complete trajectory for the robotic manipulator is generated taking into consideration the predefined “safe areas”.

Two different motion modalities are exposed by the Railab Control Platform:

- autonomous movement to a predefined target position: fixed target positions can be stored in the Railab Control Platform based on the navigation model generated from 3D data. The surgeon can command the robotic manipulator to reach these predefined target positions in an automatic way. As an example, this modality turns out to be particularly useful in order to place the endoscope in the brain tunnel. In this case, the Railab Control Platform generates robot trajectories that will move the endoscope mounted on the robotic manipulator to an absolute position in space (predefined target points);
- adjustment movements to reorient the endoscope: the robotic manipulator reacts to the commands of the surgeon by changing the final orientation of the endoscope mounted on it. As an

example, the surgeon may require the adjustment of the endoscope position inside the brain tunnel, in order to have a better view of the surgical area. In this case, the Railab Control Platform generates robot trajectories that are relative to the current position of the robotic manipulator.



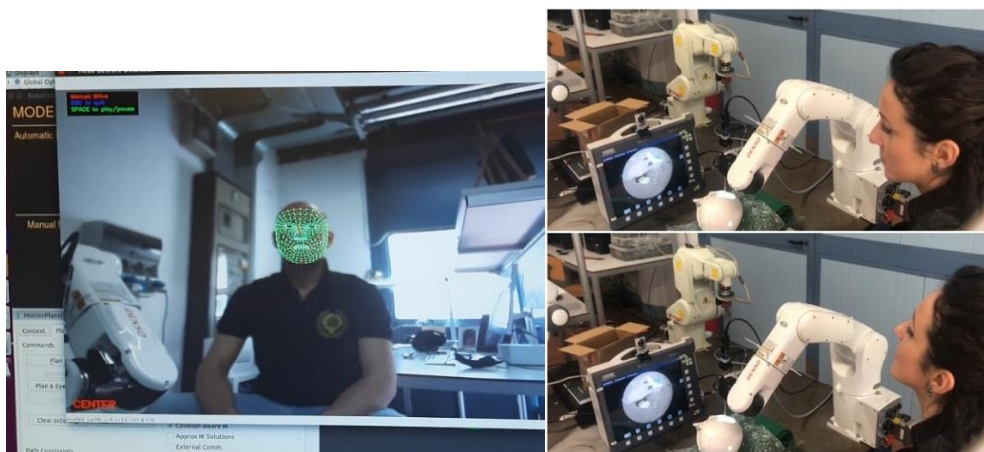
Example: predefined target points are defined from 3D data, and the Railab Control Platform generates the path to automatically move the robotic manipulator

11.3 EXPERIMENTAL RESULTS

The proposed solution has been tested on a setup prepared at Railab laboratory. The required hardware components were fully integrated from the hardware and software point of view:

- robotic arm and robot controller;
- industrial PC;
- 2D camera;
- endoscope (with monitor).

Experimental results showed the feasibility and easiness of use of the Railab solution.



Hardware setup for experimental testing phase (Railab laboratory)

12. CONCLUSIONS AND FUTURE PERSPECTIVES

The aim of this thesis was to design and develop an instrument for cerebral retraction alternative to traditional retractors, so as to allow retraction to be performed in a safer and less traumatic way.

The identification of the correct measurement system, its calibration and modification to adapt to specific needs was fundamental in proceeding with the design. This made it possible to systematically check the retraction pressure values applied by the different prototypes easily and quickly. Not only that, once the measurement system has been integrated with the metal spatula, one of the great limitations of current operating technologies has been solved, namely not having a clear and real-time view of the retraction pressures exerted. Thanks to the acquisition software and the modifications made, the instrumented spatula guarantees excellent control even for students, inexperienced surgeons or simply to limit errors related to fatigue caused by prolonging the surgery for hours.

This system can also be used for research studies, by recording the pressure exerted it is possible to evaluate the response of the tissue over time, being able to characterize the parenchyma in vivo and having a more truthful view as possible.

The design of the new spatula involved the search for a new material and the design of a new geometry. The polycarbonate used, being amorphous, guarantees the transparency necessary for the visualization of the retracted fabric over time, resolving the opacity limit given by traditional metal retractors. As regards the geometry, it has been effectively managed to modify it, creating a point with a reduced section, in such a way as to limit the pressure values exerted below the critical threshold. This spatula thus succeeds in completely replacing a traditional retractor, even without electronics which obviously increases the complexity of the system, while guaranteeing to reduce the pressure values.

Finally, the chamber was developed and consequently the klemmer type pliers to open it. The creation of the chamber responds to the need to avoid pressure concentration along the edges of the spatula which can cause lacerations and greater damage to the tissue, it also creates a corridor that protects the brain parenchyma and allows the insertion of a surgical robot avoiding contact with the healthy tissue.

The chamber in combination with the forceps has been calibrated in such a way that critical retraction pressure values are not exceeded and tissue damage is avoided. There are still several possible points to improve the designed tools.

Further developments, for example, should be addressed in the realization of the transparent polymer chamber, so as to have a continuous view of the retracted fabric.

In conclusion, this thesis has made it possible to develop a new brain retraction device, the spatula, as well as a completely innovative tool: the camera.

We then analysed brain retraction, starting from the study of the dynamic mechanical behaviour of the brain; this has therefore made it possible to improve traditional retractors, thus providing various solutions to the limits highlighted by the literature, guaranteeing the versatility necessary for such a delicate problem.

Having already completed the preclinical study phase, on a corpse and UpSim model, as well as having already started the animal study phase, will allow us to subsequently move on to the clinical phase in the operating room on a patient.

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