Available online at www.sciencedirect.com
ScienceDirect
Journal of Clinical Neuroscience xxx (2007) xxx–xxx
Journal of Clinical Neuroscience
www.elsevier.com/locate/jocn

Laboratory study

New model of bone reconstruction specially designed for skull base surgery

Patra Charalampaki [a,*], Axel Heimann [b], Laszlo Kopacz [b], Ronald Filippi [c], Islam Gawish [d], Axel Perneczky [d], Oliver Kempski [b]

[a] Department for Neurosurgery and Institute for Neurosurgical Pathophysiology, Johannes Gutenberg University Mainz, Langenbeckstr. 1, 55131 Mainz, Germany
[b] Institute For Neurosurgical Pathophysiology, Johannes Gutenberg University, Mainz, Germany
[c] Gesellschaft für Mikroneurochirurgie mbH, Gensingen, Germany
[d] Department for Neurosurgery, Johannes Gutenberg University, Mainz, Germany

Received 3 July 2006; accepted 29 August 2006

Abstract

The direct endonasal or transoral transclival approaches to the skull base permit effective, minimally invasive surgery along the clivus region. Developing long-term effective techniques to prevent cerebrospinal fluid (CSF) leaks and their consequences (infections and healing processes with long and complicated recoveries) remains a major challenge. In this study we tested a method of bone reconstruction newly developed by us, which uses a specially designed silicone plug for bone replacement after minimally invasive skull base surgery with nearly no postoperative CSF leaks. German landrace pigs were used to test the plugging efficiency of the new technique. Twelve craniotomies were performed by a subtemporal approach and subsequently the dura was opened. After these preparations the craniotomy defects were occluded with a silicone ball, which had a near spherical shape. The ball elastically adapts to the bone defect. Each pig received an intracranial pressure (ICP) catheter and a subdural catheter for later fluorescein injection. Then we increased ICP by infusion of artificial CSF and detected fluorescein leaks from the craniotomy using ultraviolet illumination and a photomacroscope equipped with appropriate filters and a charge-coupled device camera. In all pigs we increased ICP to 75–80 mmHg by infusing 25–30 mL saline containing 0.05% sodium fluorescein. The first four craniotomies had to be interrupted due to technical reasons (false craniotomy size and leak of the subdural catheter). The following eight craniotomies were 100% tight without CSF leakage. This novel medical device allows an absolutely leak-proof closure of bone defects left after minimally invasive craniotomies; no additional surgeries or other therapies were necessary. The application of the silicone plug, which is made of a cost-effective and biocompatible material, is easy and fast, making use of a specially developed toolkit.

Keywords: Bone reconstruction model; Skull base surgery; Silicone plug; CSF leakage

1. Introduction

Since the introduction of extended trans-sphenoidal or transoral transclival approaches in the early 1970s, many significant advances have been applied to this technique, particularly the addition of the endoscope as an instrument of assistance to the microscope or for direct vision.[6] However, in the transclival approach, the different methods to restore the bone (clivus) particularly for the prevention or treatment of postoperative cerebrospinal fluid (CSF) leakage, was unsatisfactory. Today, following transclival surgery the bone is normally repaired by using an abdominal fat graft replacing the absent bone, followed by a collagen sponge and a titanium mesh buttress,

* Corresponding author. Tel.: +49 6131 172039; fax: +49 6131 172274.
E-mail address: charal@nc.klinik.uni-mainz.de (P. Charalampaki).

0967-5868/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2006.08.009

which is wedged into the epidural space. Additional fat and tissue glue is placed in the sphenoid sinus if the surgery is performed trans-sphenoidally. In most cases lumbar CSF drainage is used postoperatively for 4–5 days and for 2 days an additional nasal packing is placed. This common bone reconstruction model has limits, and repeat surgery to treat CSF leakage is often necessary.[2–11]

> The closure of the skull base bone defect after skull base surgeries to avoid CSF leakage and meningitis represents the most serious and continual challenge; this is reflected in the high rate of postoperative CSF leakage that is encountered in multiple series published by big international scull base surgical centers and also known from our experience. A perfect technique has not yet been devised, despite the valiant and ingenious methods that have been suggested.[5] (Edward Laws, *Journal of Neurosurgery*, 2005)

In thinking about the very serious problems in transclival skull base surgery we searched for an easy, fast and practical application as well as a biocompatible "solution" for the human body. We developed a specially designed silicone plug from a biocompatible material, which adapts elastically to fill out the bone defect. The plug can be covered with two specially prepared thin layers: 1) to enhance the building of scar tissue in the surrounding area, and 2) to protect the surrounding environment against infections.

A pig model was designed to analyze CSF leakage after occluding craniotomies with the newly constructed silicon plug. Leakage was determined by detecting fluorescence from artificial CSF containing fluoresceine and was infused subdurally. In this study we have tested the newly designed model of bone reconstruction for use after minimally invasive trans-sphenoidal or transoral transclival surgery.

2. Material and methods

2.1. Silicone plug model and application material

Spherical- and double-lens-shaped (compressed ball) parts were made from soft, tear-proof and elastic silicone rubber (Shore hardness 28, tear strength 6.5 N/mm^2, elongation at break 700%). The silicone material we used to form the described plug is identical to the silicone material used for shunt catheters by implantation in hydrocephalus. Furthermore, a delayed leak cannot develop due to the fact that this silicon material is not known to shrink after implantation or to change its appearance in any other way.

The ball, when slightly compressed, could easily be inserted into the craniotomy defect. The implanted material can be covered with an appropriate organic and inorganic coating in order to increase adhesion to the bone tissue and protect the surrounding structures against infection. Different bacteria of the staphylococci family account for more than 75% of all CSF infections associated with silicone material such as shunt catheters.[12] Gram-negative organisms are also isolated in 15–20% of cases.[12] The key to effective prophylaxis of silicone-associated infections seems to be the prevention of initial bacterial adhesion or colonization of the foreign body surface[13] using antibiotics which act again Gram-positive and Gram-negative bacteria. This has led to the concept of antimicrobial device impregnation or coating with such antibiotics.[12,14,15] We used an impregnation technique to incorporate antibiotics[13] (rifampin for Gram-positive and sparfloxacin for Gram-negative bacteria) in the silicone plug and tested the antibiotic release in vitro for 45 days (Fig. 1). We compared the bacterial colonization between silicone plugs, which were impregnated and those which were not impregnated with antibiotics. The results showed that the impregnated silicone plugs prevent the spreading of micro-organisms in that they dis-

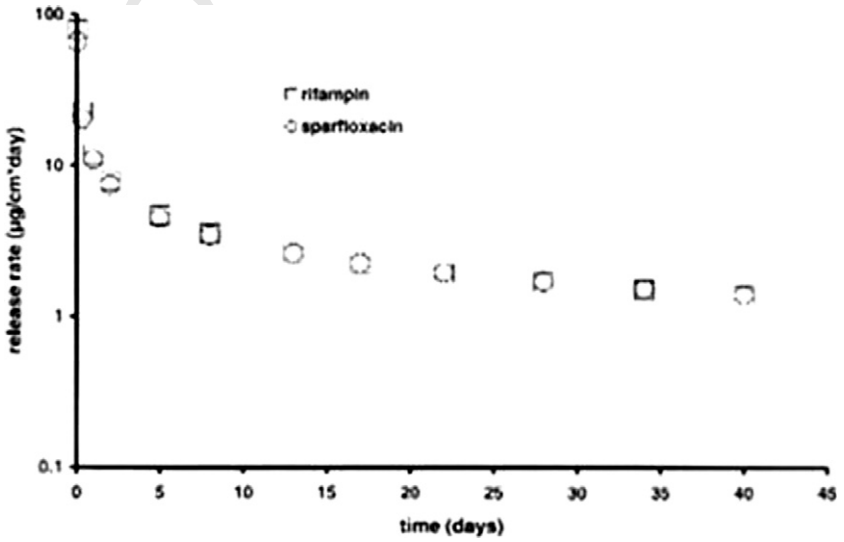

Fig. 1. Antibiotic release of a silicone plug impregnated with rifampin and the quinolone sparfloxacin.

Please cite this article in press as: Charalampaki P et al., New model of bone reconstruction specially designed ..., *J Clin Neurosci* (2007), doi:10.1016/j.jocn.2006.08.009

charge antibiotics over a long period of time into the surrounding area (Fig. 2). Moreover, the impregnated silicone plug should be suitable to prevent contamination of the material during implantation, not only by preventing colonization but also by killing bacteria pre-existing in the surgical field.

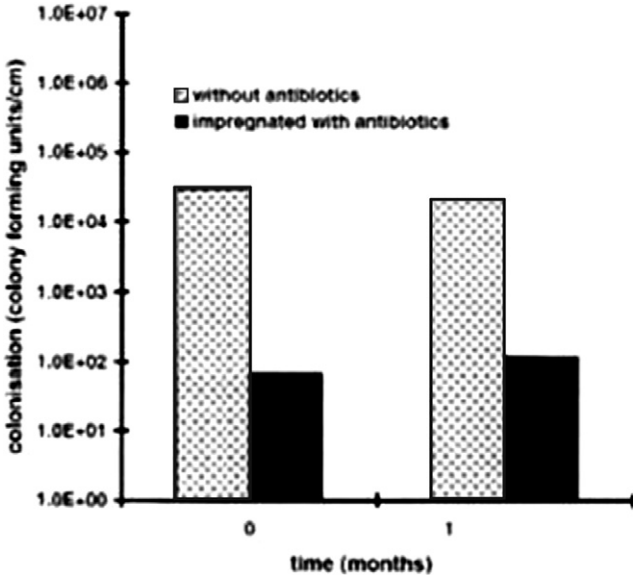

Fig. 2. Colonization of silicone plug with *Staphylococcus epidermis*.

Furthermore, all elements can be supplied with cell growth promoting compounds by dipping, spraying or steaming.

In order to facilitate the applicability of these elements (which also is easily done with a set of tweezers) both an applicator and an extractor were designed. These instruments, which are sterilizable and therefore re-useable, are made entirely of metal and provided with a "gun handle"; they have appropriate dimensions for endoscopy or microsurgery and are easily adjustable to the employed elements, or they are self-adjusting.

The functional principle of the applicator is based upon the retaining of a pre-packaged sealing material as well as its sufficient and necessary deep insertion into an opening, which is to be sealed/filled by the use of a guide tube and a push rod. The pre-packaging of the sealing element into a tube-shaped, cylindrical, thin-walled plastic part with adequate diameter and standardized retainer shaft, assures fast and precise handling and efficient replacing of the sealing elements as well as compliance with the maximal position-

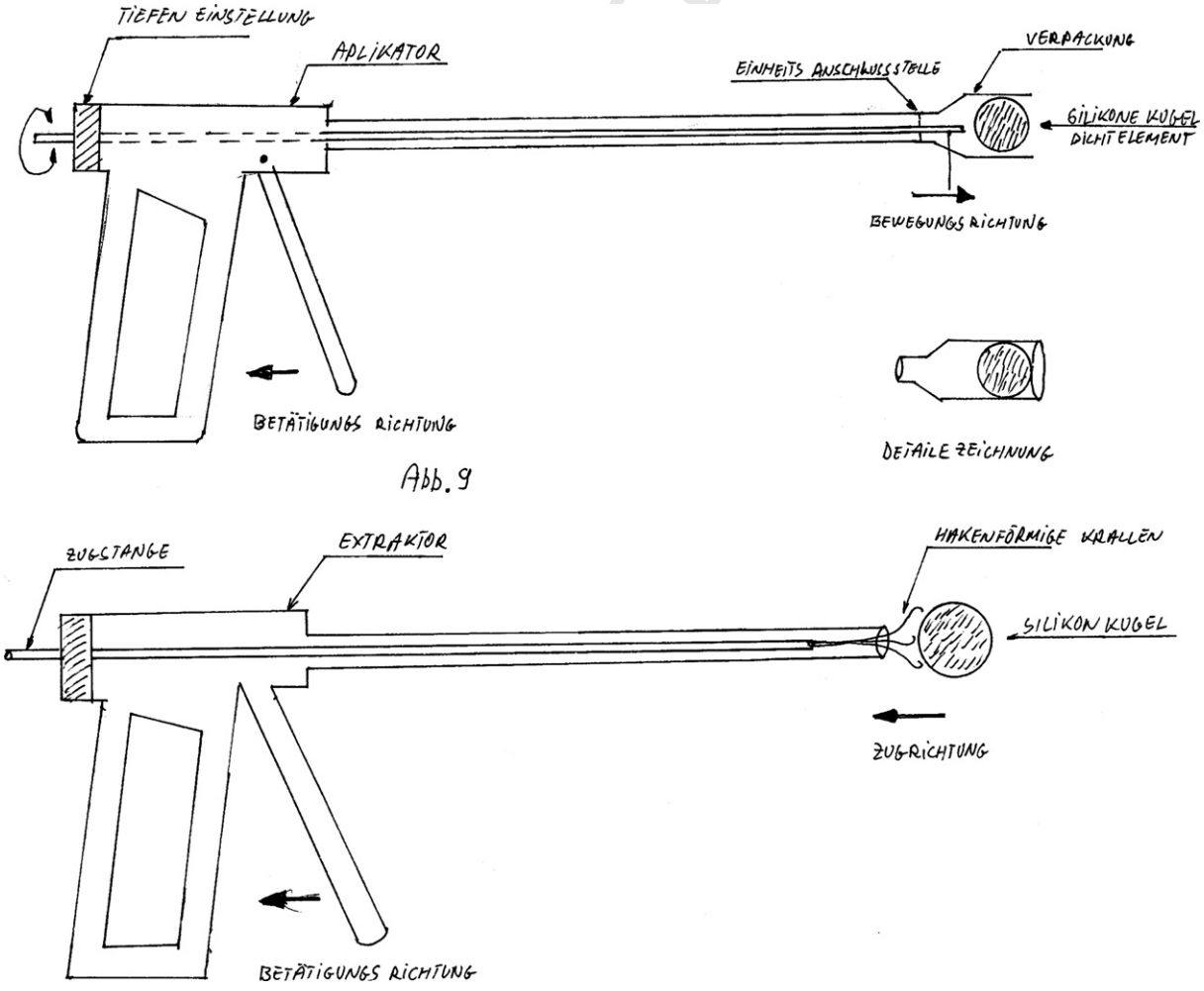

Fig. 3. Micro-instruments for positioning the silicone plug in the bone defect.

Please cite this article in press as: Charalampaki P et al., New model of bone reconstruction specially designed ..., *J Clin Neurosci* (2007), doi:10.1016/j.jocn.2006.08.009

ing depth which is determined by the length of the packaging.

The functional principle of the extractor is based upon the grabbing, and subsequently the sufficient and necessary extraction of the sealing element from the sealed/filled opening. The pull rod consists of a gripper containing at least three symmetrical opening claws, which in a resting position are folded inside a guide tube. When the gripper is activated the curved claws open and move forward so far as to enable the grabbing and the extraction of the sealing element. The hooked claws of the gripper are pushed into the sealing element and retracted by tractive force. This functional principle ensures that the element cannot be further pushed in the direction of the brain and also cannot slip from the gripper (Fig. 3).

3. Experiments

To test the plug stability in the bone defect we created a 6-mm borehole on the cribriform lamina in a human skull and closed the defect with a silicone plug of 8-mm diameter. We filled the surface of the front skull base with water and examined the movement of the plug. We introduced an air pistol transnasally and injected air under pressure (5 bar) through the defect. Water lying at the surface of the cribriform lamina showed no air bubbles and the silicone plug showed also no evidence of displacement. This short experiment showed that sudden rises of intracranial pressure (ICP), such as sneezing, could not expel the plug from its position.

Afterwards, to test the plug efficiency, German landrace pigs (n = 6; mean weight, 30 kg) were used. Under general anesthesia, with intravenous infusion of midazolam and dipidolor, we performed a subtemporal approach and not a transoral transclival approach. This was necessary owing to the anatomical nature of pigs (the distance between the mouth entrance and clivus is too long for clinical microinstruments; the distraction capacity of the mouth is too small), which does not allow interaction with microinstruments. We performed 12 craniotomies and opened the dura. Initially, the four boreholes were performed with a 7-mm Rosen burr drill and were occluded with silicone balls, which had a near-spherical shape (8 mm diameter) and formed elastically to fill the bone defect. The next eight holes were drilled with a diamond drill, 6-mm in diameter, and filled out with silicone balls 8 mm in diameter. Each pig received an ICP catheter, one frontal intracerebral and another frontal subdural for later fluorescein injection. Both catheters were fixed on the dura with glue to avoid fluorescein leaks from these small bone defects (Fig. 4). Then we increased ICP by infusion of artificial CSF (saline with 0.05% fluorescein) and detected fluorescein leaks from the subtemporal craniotomy using ultraviolet illumination and a photomacroscope equipped with appropriate filters (excitation: 450–490 nm, dichromatic mirror: 510 nm, emission: >515 nm), and a charge-coupled device (CCD) camera (Fig. 5).

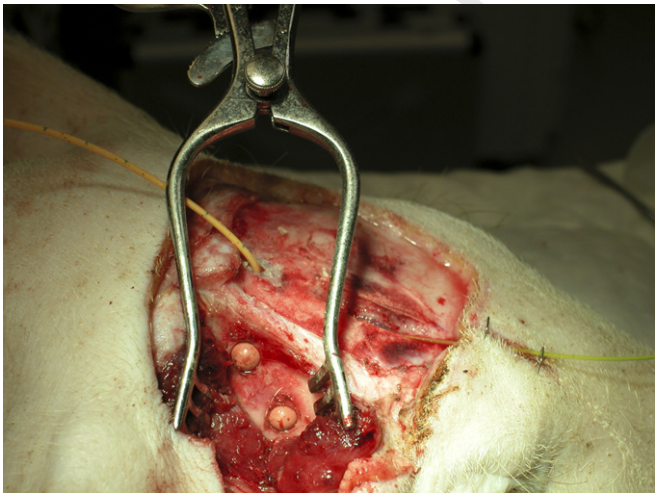

Fig. 4. Each pig received an intracranial pressure catheter, one frontal intracerebral and another frontal subdural for later fluorescein injection. Both catheters were fixed on the dura with glue to avoid fluorescein leaks from these small bone defects.

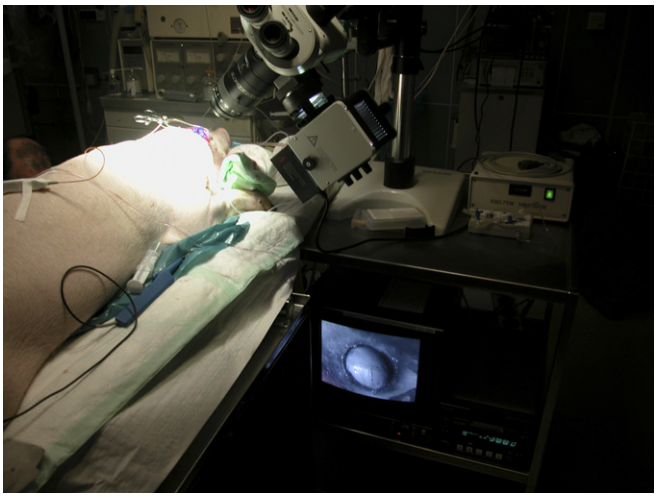

Fig. 5. Detection of fluorescein leaks from the subtemporal craniotomy using ultraviolet illumination and a photomacroscope equipped with appropriate filters and a charge-coupled device camera.

4. Results

We performed the first two craniotomies with a 7-mm drill and occluded the bone defect with an 8-mm silicone plug. We were not able to finish this experiment because after increasing the ICP to 17–20 mmHg a fluorescein leak appeared through the subdural catheter. We had to, Therefore we had to interrupt the experiment (Fig. 6a,b). The reason for the leak was an incorrect fixation of the catheter at the dura. We performed the next two craniotomies using a 7-mm drill and occluded the bone defect with an 8-mm silicone plug. After increasing the ICP to 40–45 mmHg, we again detected fluorescein around the surface of the

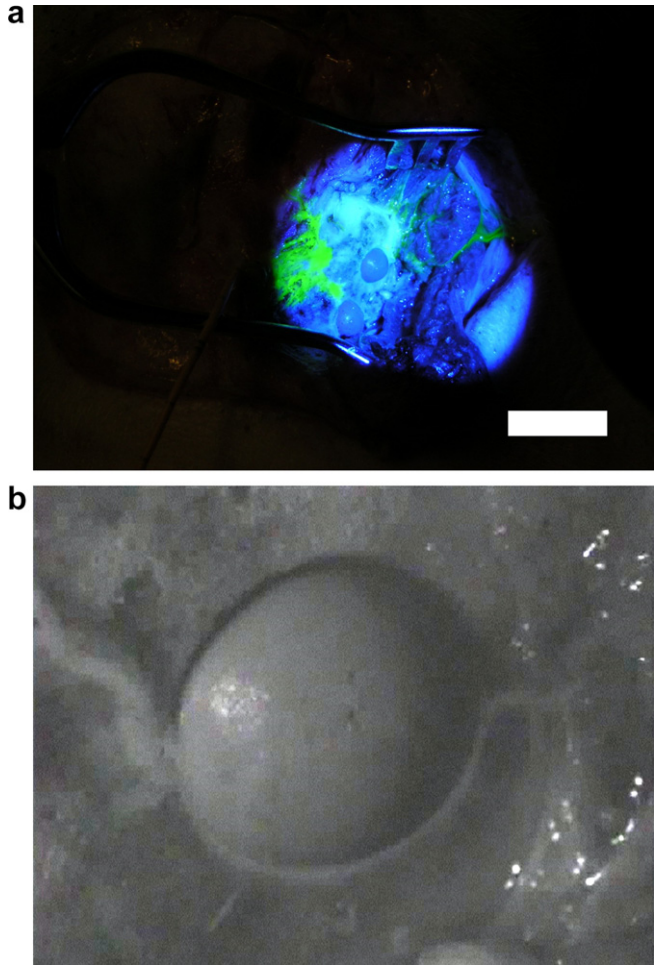

Fig. 6. (a,b) Fluorescein leak appeared, coming through the subdural catheter.

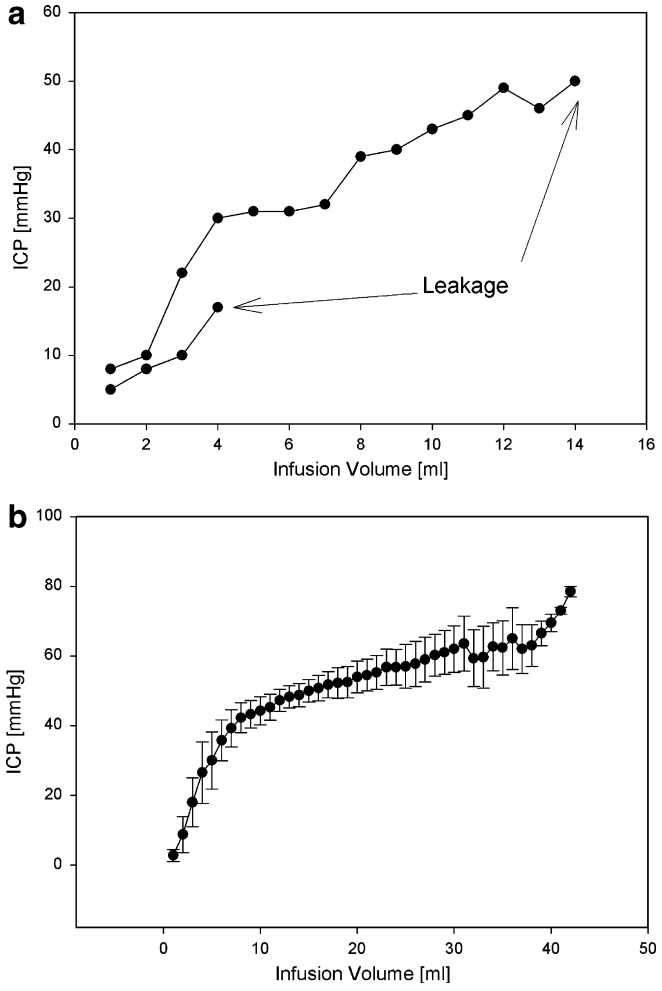

Fig. 8. (a,b) During the first four craniotomies (a) fluorescein leak appeared. During the next eight craniotomies (b) fluorescein was not detected.

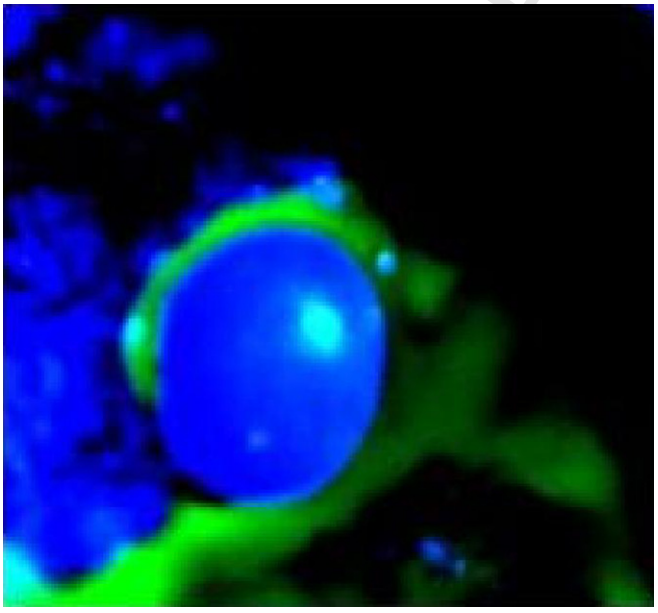

Fig. 7. Detection of fluorescein around the surface of the plug, after increasing the intracranial pressure to 40–45 mmHg. The craniotomy of 7-mm diameter was too big to be filled out by the 8-mm diameter silicone plug.

plug. This experiment had to be interrupted as well (Fig. 7). We found the reasons for the leakage was due to the diameter of the craniotomy being too large; it could not be filled completely by the silicone plug. As well, an irregular shape on the surface of the craniotomy (a Rosen burr drill caused bone grooves) allowed fluorescein to leak (Fig. 8a,b).

We decided to perform the next eight craniotomies with a smaller (6 mm diameter) diamond drill to achieve a smooth shape on the craniotomy surface. Furthermore, we chose the diameter of the ball at 120% of the existing craniotomy. The occlusion of the bone defects were made by 8 mm silicone balls. After increasing ICP to 75–80 mmHg, we did not detect fluorescein at the surface of any of the craniotomies. The bone defects were occluded with 100% safety; CSF leakages were not detected (Fig. 9a,b).

5. Discussion

The direct endonasal or transoral transclival approaches to the skull base provide an effective minimally invasive

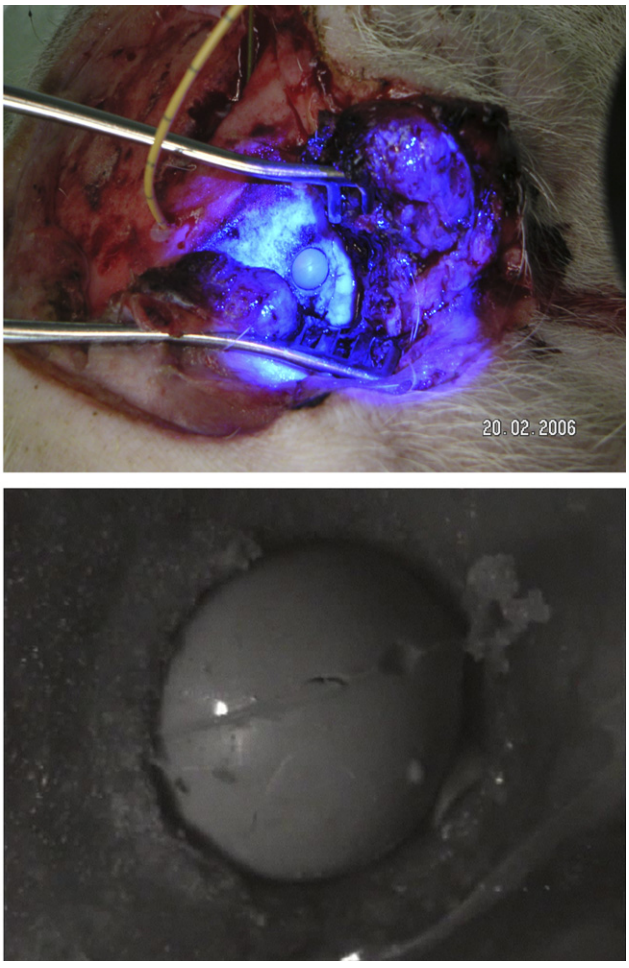

Fig. 9. (a,b) Craniotomies performed with 6-mm diamond drill and occlusion with an 8-mm silicone ball. After increasing the intracranial pressure to 75–80 mmHg, fluorescein was not detected.

means for preparing processes along the clivus region. The major challenge remains: developing consistently effective techniques to prevent cerebrospinal fluid (CSF)-leaks and their consequences (infections and long healing processes with long and complicated recoveries). Reconstruction today is usually performed with muscle or fat tissue and titanium plates, which lead to additional traumatic wounds and sometimes to associated complications such as infections or neurological disorders.[2,3,5,11]

We have found that bone reconstruction must be performed with a material: (i) whose origin is not traumatic for the patient, that is, not requiring further surgery for the removal of fat or muscle; (ii) which is easily applicable to the bone defect; (iii) in which the consistency is formable and elastic, allowing it to completely fill the surrounding surface of the craniotomy; (iv) which can be covered with a specially prepared thin layer to enhance the building of scar tissue in the surrounding area; (v) which is built from a material that is biocompatible with the human body; and (vi) which guarantees acute and longer-term tightness of the bone defect without additional surgical or conservative therapies. Respecting these points, we developed a bone reconstruction model for craniotomy defects at the skull base, which is made of biocompatible silicone for medical use. This innovative new implantable medical device allows tight closure of the bone after its placement inside the craniotomy defect without exerting additional pressure onto the brain. The product could be used for closing bone defects after trans-sphenoidal or transoral transclival surgery and could achieve a postoperative condition, which is both absolutely free of CFS leakage and in which a pathogen invasion of bacteria into the intracranial space is not possible.

As shown in our results, the closures of the defects can be performed safely if the diameter of silicone plugs exceeds 120% of craniotomy diameter. But what happens if the bone defect is not circular and the diameter of the hole is larger than 8 mm, dissimilar from our experiments? As we know, in order to reach a satisfactory craniotomy in the clivus region, the bone defect must be extended approximately 2 cm in length and 1.5 cm in width.[3,4]

A spherical form with these diameters would project over the clivus inner surface on the brainstem, causing a life-threatening compression of the brainstem. Thus, we considered more ellipsoid shapes for the covering of defects which are not circular. Silicone plugs with a diameter of 120% compared to the existing craniotomy were selected, so that the slightly squeezed plugs could be easily placed into the existing opening.

Testing of these elements demonstrated very good sealing ability. The sealing in the non-circular openings depended on the adaptability of the spherical flexible element as well as sufficient radial contact pressure in the narrow circular surface. In addition, the sealing effect was improved by the smooth surface. Concerning these observations, we thought to create another form, lens-like, ellipsoid or quadrangular with round corners. A nugget shape has the advantage over a ball shape in that it exhibits a relatively large diameter with a relatively small thickness. By that means, a protrusion over the bone edges and compression of nerval structures can be prevented. With a pillow-shaped plug, in particular, an irregular opening can be occluded closely. Additionally, we observed that a circular sealing-rim around the plug improves the tightness in these irregular bone defects, because the radial contact pressure is increased without inappropriate pressure enhancement. Due to the above, variations of the implants have to be produced industrially for openings with different shapes.

De Diviitis et.al. showed that in order to reach a satisfactory craniotomy in the clivus region, the bone defect must be extended approximately 2 cm in length and 1.5 cm in width.[4] It would be conceivable to have a medical set with different ellipsoids elements graduated in diameters. The smallest form would have a width of 1.5 cm × 1.2 cm (120%) with a length of 2 cm × 1.2 cm (120%) and in 2-mm steps to 3 cm × 1.2 cm (120%) and 2.7 cm × 1.2 cm (120%). The material would have an elastically and well formable surface with Shore hardness

of 25–30 and a core with Shore hardness of 50–60 for better stabilization by positioning in the bone defect. Furthermore, all these elements can be covered with suitable organic and inorganic coatings to increase adhesion at the bone surface, as well as cell growth, favouring connections by dipping, spraying, vaporizing or sputtering. Essential characteristics of the invention are thus the sealing of a bone defect by a pre-compressed flexible sealing material.

In order to facilitate the applicability of these elements (which also is easily done with a set of tweezers) both an applicator and an extractor were designed. These instruments, which are sterilizable and therefore re-useable, are made entirely of metal and provided with a ''gun handle''. They also have appropriate dimensions for endoscopy or microsurgery and are easily adjustable to the employed elements or they are self-adjusting. The advantages are that the skull base is reconstructed only with this material and without additional withdrawal of fat, muscle, etc.

The closure is completely tight and the duration of surgery, in cases of uncomplicated applications, is very short. In cases of intraoperative safe sealing of the skull base, such tools as nasal tampons, lumbar drainage, additional surgeries for the withdrawal of muscle or fat, complications and side effects can be avoided as patients are able to breathe freely and therefore can be mobilized immediately after the surgery. The public health service profits by the shortening of hospitalization stays and faster discharges.

6. Conclusion

This novel medical device allows a leak-proof closure of bone defects left after minimally invasive craniotomies; no additional surgery or other therapies would be necessary. The handling during its application is easy and fast using a specially designed toolkit. The device itself is made of a cost-effective and biocompatible material.

7. Uncited reference

[1].

Acknowledgement

We state that we received no financial support to analyze this data and we have no financial interest in any materials or devices described in our submission. We thank our neuroradiological technical assistant Mrs. Janice Roberts for her help in preparing the manuscript.

References

1. Guity A, Young PH. A new technique for closure of the dura following transsphenoidal and transclival operations. Technical note. *J Neurosurg* 1990;**72**:824–8.
2. Arita K, Kurisu K, Tominaga A, et al. Size-adjustable titanium plate for reconstruction of the sella turcica. Technical note. *J Neurosurg* 1999;**91**:1055–7.
3. Crockard HA. Transoral surgery: some lessons learned. *Br J Neurosurg* 1995;**9**:283–93.
4. de Divitiis O, Conti A, Angileri FF, et al. Endoscopic transoral-transclival approach to the brainstem and surrounding cisternal space: anatomic study. *Neurosurgery* 2004;**54**:125–30, discussion 130.
[5] J.R.Dusick, Esposito F, Kelly DF, et al. The extended direct endonasal transsphenoidal approach for nonadenomatous suprasellar tumors. *J Neurosurg* 2005;**102**:832–41.
6. Laws ER, Kanter AS, Jane Jr JA, et al. Extended transsphenoidal approach. *J Neurosurg* 2005;**102**:825–7, discussion 827–8.
[7]C.S.Ogilvy, Barker 2nd FG, Joseph MP, et al. Transfacial transclival approach for midline posterior circulation aneurysms. *Neurosurgery* 1996;**39**:736–41, discussion 742.
[8]R.Reisch, Bettag M, Perneczky A. Transoral transclival removal of anteriorly placed cavernous malformations of the brainstem. *Surg Neurol* 2001;**56**:106–15, discussion 115–116.
[9]G.J.Kaptain, Vincent DA, Laws Jr ER. Cranial base reconstruction after transsphenoidal surgery with bioabsorbable implants. *Neurosurgery* 2001;**48**:232–3, discussion 233–234.
10. Kumar A, Maartens NF, Kaye AH. Reconstruction of the sellar floor using Bioglue following transsphenoidal procedures. *J Clin Neurosci* 2003;**10**:92–5.
11. Jho HD, Ha HG. Endoscopic endonasal skull base surgery: Part 3 – The clivus and posterior fossa. *Minim Invasive Neurosurg* 2004;**47**:16–23.
12. Kohnen W, Jansen B. Polymer materials for the prevention of catheter-related infections. *Zentralbl Bakteriol* 1995;**283**:175–86.
13. Kohnen W, Kolbenschlag C, Teske-Keiser S, et al. Development of a long-lasting ventricular catheter impregnated with a combination of antibiotics. *Biomaterials* 2003;**24**:4865–9.
14. Schierholz J, Jansen B, Jaenicke L, et al. In-vitro efficacy of an antibiotic releasing silicone ventricle catheter to prevent shunt infection. *Biomaterials* 1994;**15**:996–1000.
15. Elliott T. Intravascular catheter-related sepsis–novel methods of prevention. *Intensive Care Med* 2000;**26** (Suppl.1):S45–50.