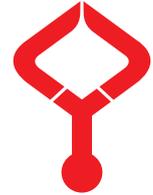


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Experimental Research

J. Exp. Clin. Med., 2015; 32(2): 77-82
doi: 10.5835/jecm.omu.32.02.007

Comparison of the efficiency, side effects and complications of the synthetic dural grafts: Beriplast and Tissudura

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ARTICLE INFO

ABSTRACT

Article History

Received 11 / 03 / 2015

Accepted 10 / 05 / 2015

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The purpose of the study was to compare human fibrinogen-thrombin-based liquid dural graft; Beriplast® (Behring, Malburg, Germany) and collagen-based dural graft; Tissudura® (Baxter, Heidelberg, Germany) in terms of efficiency, side effects and complications. Thirty Sprague Dawley rats were used in this experimental study. A burrhole was opened on the left parietal bone of each subject and experimental dural defect was created. While 10 subjects were in sham group without any dural defect repair, dural defect was repaired by Beriplast in 10 subjects, by Tissudura in 10 subjects. After twenty-one day follow-up, edema, gliosis and inflammatory cell infiltration in the parenchyma, foreign body reaction in the bone, fibrosis in the epidural space and dura were evaluated histopathologically. Beriplast caused much more severe inflammation on cortex. When we compared Tissudura group with the sham group in terms of parenchymal edema and gliosis, the difference was not significant. On the other hand, we have found a significant increase in cortical parenchymal edema in Beriplast group. The last generation dural grafts result in different degrees of the tissue reaction. Severe inflammatory reaction can provide more satisfactory results in terms of watertight dural closure but on the other hand, the same reaction can be a disadvantage to the surrounding tissue.

Keywords:

Beriplast
Dural defect
Dural graft
Tissudura

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1. Introduction

The leading causes of the cranial dural defects are head traumas, neurosurgical approaches, tumoral infiltrations, infections, congenital fistulas and empty sella syndrome (Greenberg, 1994).

Duraplasty is a kind of procedure in which dura mater can't be sutured primarily and needs to be covered by the grafts. In the case of inadequate duraplasty, complications such as cerebrospinal fluid (CSF) fistulas, infections, pseudomeningoceles and prolonged hospitalization can be seen. Increased morbidity even mortality can also be detected due to these complications. There has been an important issue in modern neurosurgical clinics in terms of avoiding these

complications. For that reason, closing dura mater needs to be a must by duraplasty in watertight form.

Today, Tissudura (Baxter, Heidelberg, Germany) and Beriplast (Behring, Malburg, Germany) are often used as dural grafts in neurosurgery. Tissudura is a natural collagen biomatrix. It is derived from heterogenous Achilles tendon (Esposito et al., 2008). It regenerates the anatomy, prevents adhesions, encapsulation, CSF fistulas by the help of biological well-adjusted collagen form (Esposito et al., 2008). It maintains cell penetration and spreading of cells on matrix. These cells grow up, differentiate metabolically and form into dura mater tissue. Collagen fibrils in network like matrix transform to fibrous layers, which are rich in cells,

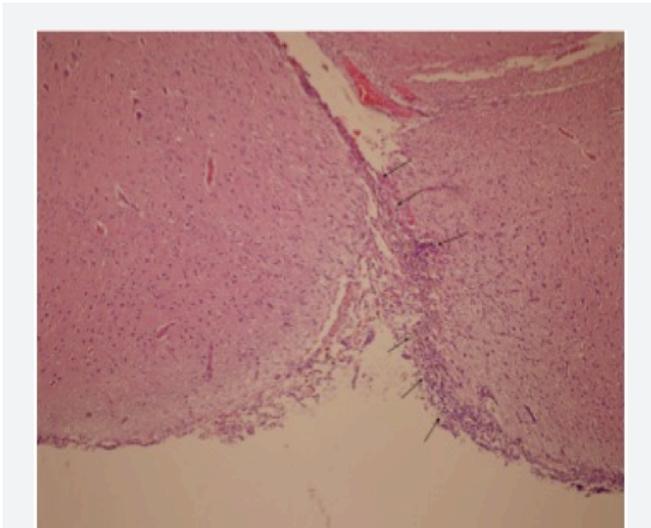


Fig. 1. Inflammation cells (arrows) in parenchymal tissue after staining with H&E

elastic, watertight and also stretch-resistant, in the week of 16 (Narotam et al., 2004; Esposito et al., 2008). It is easily used and gets along with complex surfaces with giving chance to natural dural regeneration. It can be used by both of its wet and dry surfaces, maintains primary liquid isolation with fibrin glue and can be applied sutureless (Narotam et al., 2004; Esposito et al., 2008).

Beriplast consists of factor XIII and thrombin, which are the blood coagulation factors, and also aprotinin and calcium chloride, which are known as antifibrinolytic agents (Dunn and Goa, 1999). It helps hemostasis and wound healing (Eberhard et al., 2006). On behalf of that it is clinically used as drug carrier as physiological tissue glue in the treatment of minor targets of cancer. It is obviously informed that the usage of anti-carcinogen drugs is more efficient with beriplast (Handa and Koyama, 1989; Matsuoka et al., 1996). Easy application, natural dura regeneration and easy penetration to complex surfaces because of the liquid form are its important properties (Nistor et al., 1997; Schelling et al., 1998).

In this experimental study, we aimed to compare the efficiency, side effects and complications of these two synthetic materials.

Table 1. The histopathological score scale of inflammation, foreign body reaction, edema and gliosis of the H&E stained preparations

	Inflammation	Foreign body reaction	Edema	Gliosis
0	no inflammation	absent	absent	absent
1	mild	limited	mild	mild
2	moderate	extensive	moderate	moderate
3	severe	very severe	severe	severe

2. Material and methods

This study has the approval of the Ethics Committee of Animal Experimentations from Ondokuz Mayıs University. We performed this study at Ondokuz Mayıs University Experimental Animal Research Center by using 30 Sprague Dawley rats, which were 300-400 gram in weight and 16-20 weeks old in age.

The subjects were divided into three groups (Beriplast;

group B, Tissudura; group T and sham; group S) of 10 rats in each. Each group was kept in separate cages, in their natural environment without food and water restrictions. The rats were fasted for 12 hours before the experimental surgery and were only allowed to drink water.

In this study, rats were sedated preoperatively by giving 10 mg/kg xylazine (Rompin-Bayer) and 80 mg/kg ketamine hydrochloride (ketamine on-Parke Davis), intraperitoneally. Rats were taken to the operating table after anesthesia. Skin antisepsis was provided with 10% povidone iodine solution after the surgical site shaving. 1.5 cm length incisions of the skin and subcutaneous tissue were performed on the left parietal region. A burrhole was created on the parietal bone with the help of surgical microscope, high-speed drill, 3 mm ball-end and dura mater was found. 3 mm incision was made on dura mater by using 11-no scalpel. 0.5 cc Beriplast and 0.5x0.5 cm Tissudura was placed on the dural defect in Group B and Group T, respectively. Group S was determined as sham and was not used any material in place of dural defect. The skin and subcutaneous tissues were sutured with silk 4/0 after confirming hemostasis. 10% povidone-iodine solution was applied to the incision areas of all cases.

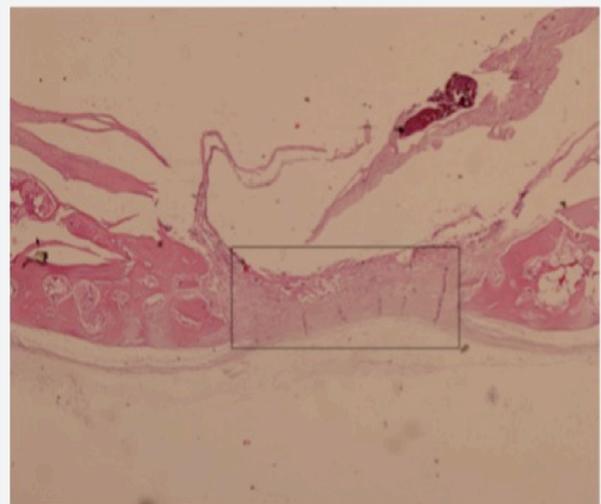


Fig. 2. Fibrosis in bone tissue is shown in the rectangle after staining with H&E

The rats were placed in cages with warming. Body temperature was kept constant and 2 mg/kg paracetamol was given for 3 days, orally. Rats were followed for 21 days for evaluation of general behavior, neurological signs, mobility and signs of infection. Abnormal posture and motor deficits, redness in the surgical area, the appearance of infection symptoms, decreased feed and water consumption were determined as the study exclusion criteria.

All rats were decapitated under anesthesia at 21st day of the study and both cerebral hemispheres were removed en bloc with the dura.

Histopathological evaluation

Cerebral parenchyma and dura mater were fixed with formalin. Transverse sections of the cerebral tissue and dura mater samples, which were taken from the lesion area, were embedded in paraffin blocks. The parietal bone was decalcified by allowing to stand for five days in acid solution. Transverse

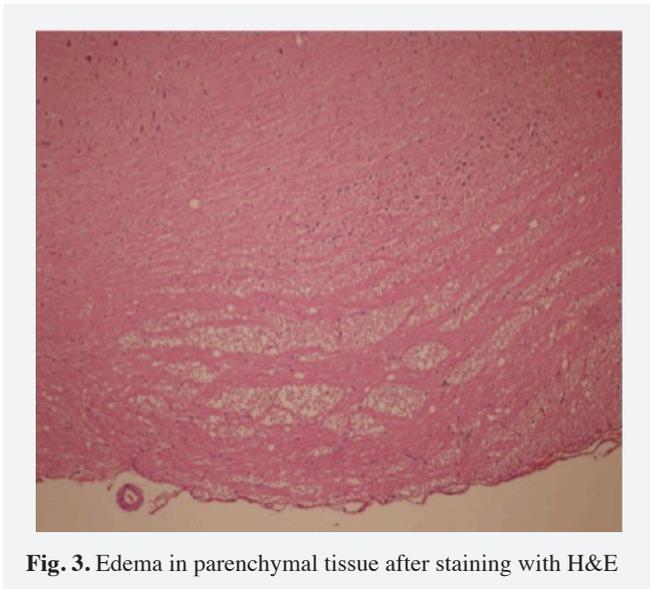


Fig. 3. Edema in parenchymal tissue after staining with H&E

sections of bone tissue were embedded in paraffin blocks. five micron sections were taken from paraffin-embedded and were stained with H & E and luxol fast blue histochemical dyes. Histological evaluation was done by a pathologist by using light microscopy. Inflammation, foreign body reaction, edema and gliosis were evaluated (Fig. 1, 2, 3 and 4) and scored (Table 1).

group B, 8 of the 10 subjects (80%) had mild inflammation. One of them showed abscess formation, which was independent from the usage of Beriplast. Mild inflammation was observed in 6 out of the 10 subjects (60%) in group T. When groups were compared, inflammation and fibrosis were found significantly higher in group B ($p < 0.05$).

Edema of Parenchymal tissue

In terms of edema, it was not possible to differentiate the influence of the trauma to dura mater from the effect of the synthetic dural graft usage. One out of 10 subjects (10%) in Sham group showed mild edema. Seven of the 10 subjects (70%) in group B and 3 of the 10 subjects (30%) in group T had mild edema. When groups were compared, the development of edema was statistically significantly higher in group B ($p < 0.05$). There was no significant difference between group T and S ($p > 0.05$).

Gliosis of Parenchymal tissue

Gliosis around the surgical field, which developed because of the primary surgical trauma or secondary to foreign body reaction, was evaluated. While we found mild gliosis in two out of the 10 subjects (20%) in group S, three subjects showed mild gliosis in each group B and T (30%). When we compared group B with groups T and S, a statistically significant difference was detected ($p < 0.05$). On the other hand, there was no statistically significant difference between group T and S ($p > 0.05$).

Table 2. The distribution of the histopathological signs in the Sham group

	Parenchyma				Bone		
	Inflammation	Edema	Gliosis	Foreign body reaction	Inflammation	Foreign body reaction	Fibrosis
1	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-
3	2	-	1	1	1	1	+
4	-	-	-	-	1	1	+
5	-	-	-	-	-	-	-
6	1	1	1	-	-	-	+
7	-	-	-	-	-	-	+
8	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-

Statistical evaluation

Statistical evaluation was performed using an alpha level of 0.05 to determine statistical significance. The data were presented as percentage. Groups were compared using the Kruskal Wallis test and a chi-square analysis. SPSS software version 15.0 was used for statistical testing.

3. Results

Any exclusion criterion was not observed during the study. The results of the histopathological examination of the groups are shown in Tables 2, 3 and 4.

Inflammation of Parenchymal tissue

Inflammation and fibrosis, which occurred in the defective dura, were evaluated. Two out of 10 subjects (20%) in group S showed mild and moderate inflammation, respectively. In

Foreign Body Reaction of Parenchymal tissue

One of the subjects in every three groups (10%) had very limited foreign body reaction. Group B and T showed a statistically significant difference when compared with group S ($p < 0.05$). There was no significant difference between group S and T ($p > 0.05$). It was group B that created the difference.

Inflammation of bone tissue

Two subjects (20%) showed mild inflammation in group S. While moderate inflammation was seen in one of the 10 subjects (10%), eight subjects (80%) had mild inflammation and one subject (10%) had no significant inflammation in group B. In group T, four subjects (40%) showed mild inflammation and 1 subject (10%) showed moderate inflammation. Bone tissue inflammation was found significantly higher in group B compared with the groups S and T ($p < 0.05$).

Table 3. The distribution of the histopathological signs in Berioplast group

	Parenchyma				Bone		
	Inflammation	Edema	Gliosis	Foreign body reaction	Inflammation	Foreign body reaction	Fibrosis
1	1*	1	1	-	1	1	+
2	-	-	-	-	-	-	-
3	1	1	-	-	1	1	+
4	1	1	1	1	1	1	+
5	1	1	-	-	2	3	+
6	1	1	1	-	1	2	+
7	1	1	-	-	1	1	+
8	1	-	-	-	1	1	+
9	-	-	-	-	1	1	+
10	1	1	-	-	1	-	+

* abscess (independent with Berioplast)

Foreign body reaction of bone tissue

Two of 10 subjects (20%) showed a limited degree of foreign body reaction in group S. Six subjects (60%) had limited degree, one subject (10%) had extensive and one subject (10%) had very severe foreign body reaction in group B. In group T; four subjects (40%) were without foreign body reaction, four subjects (40%) were with limited and two subjects (20%) were with extensive foreign body reaction. There was statistically significant difference when group B and T were compared with the group S and among themselves ($p < 0.05$).

Bone Tissue Fibrosis

Bone tissue fibrosis was observed in four out of 10 subjects (40%) in group S. While 9 of 10 subjects (90%) had bone tissue fibrosis in group B, it was detected in all of the subjects in group T (100%). Group B and T were significantly different from the group S ($p < 0.05$).

4. Discussion:

Dura mater is the outermost layer of the meninges. It provides a mechanical barrier between the CSF and the external environment and protects the nervous system from infection (Narotam et al., 2004; Esposito et al., 2008; Stendel et al., 2008).

The integrity of the dural barrier can be disrupted by

trauma, neoplastic infiltration and surgical interventions (Aykan et al., 2002; Mukai et al., 2008; Chappell et al., 2009). In neurosurgery, dural barrier disruption causes major complications such as CSF fistula, meningitis, ventriculitis, deep-seated abscess infections, pseudomeningocele and / or related nerve entrapment syndromes and intracranial hypotension (Narotam et al., 2004; Esposito et al., 2008). For that reason, it is very important in neurosurgery to repair dural defects water tightly (Sekhar et al., 2001; Malliti et al., 2004). Watertight dural repair can be difficult because of the lack of adequate dural tissue, the inability in demonstrating of the dural margin to be repaired clearly and neoplastic infiltration of the dura.

There are lots of methods to repair dural defect water tightly. Most preferred and also the best method is primary suturing of the dural defect in the presence of enough dural tissue and surgical exposure. With this method, the autologous tissue is closed in a closest way to its own natural (Topsakal et al., 1993; Takcı et al., 2001; Lage et al., 2006; Narotam et al., 2009). If primary closure is impossible, duraplasty, which means the usage of alternative products to dura mater, can be performed.

Alternative dura grafts can be examined in four subgroups: allografts, autologous grafts, non-autologous animal grafts (xenografts) and synthetic grafts. Allograft is the transplant of the tissue from one individual to another of the same species with a different genotype. Autologous grafts are tissues such as galea, fascia, muscles tissue and adipose tissue, which are taken from the patient himself. The most important advantages are not carrying a risk of infection of another host, lower cost and not forming any immune reaction. The disadvantages are not being always sufficient, need for a second surgical procedure and pain, cosmetic problems and risk of infection at the secondary surgical site. We can find animal grafts easily and in a large amount but on the other hand, they can create immune reactions, cause severe infections and adhesions. The advantages of synthetic grafts are easy application, no need of suturing, elasticity, lower risk of infection and immune reaction (Nussbaum et al., 1989; Hatanaka, 1992; Narotam et al., 1993; Bhatia et al., 1995; Narotam et al., 1995; San-Galli et al., 1996; Nistor et al., 1997; Alleyene et al., 1998; Schelling et al., 1998; Vinas et al., 1999; Kelly et al., 2001; Narotam et al., 2004; Knopp et al., 2005; Dietemann et al., 2005; Cappabianca et al., 2006; Shimada et al., 2006; Esposito et al., 2008). The most important disadvantage of these grafts is their high cost.

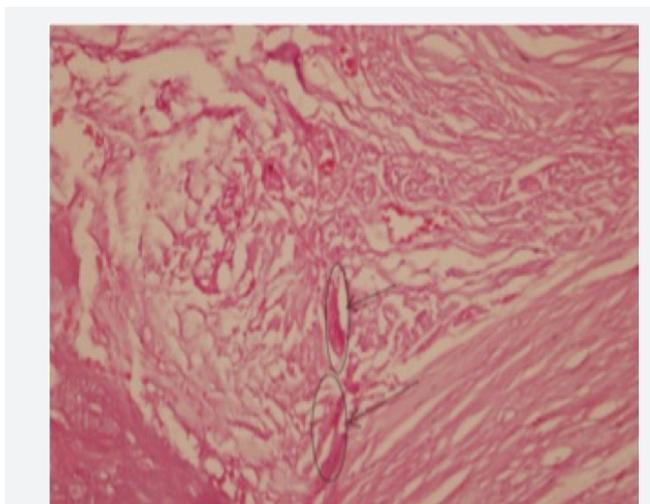


Fig. 4. Foreign body reaction in bone tissue is shown in the circle after staining with H&E

Table 4. The distribution of the histopathological signs in Tissudura group

	Parenchyma				Bone		
	Inflammation	Edema	Gliosis	Foreign body reaction	Inflammation	Foreign body reaction	Fibrosis
1	1	1	-	-	2	2	+
2	1	1	-	-	1	1	+
3	-	-	-	-	1	1	+
4	-	-	-	-	-	1	+
5	1	-	1	-	1	1	+
6	1	-	1	1	1	2	+
7	1	1	-	-	-	-	+
8	1	-	1	-	-	-	+
9	-	-	-	-	-	-	+
10	-	-	-	-	-	-	+

First generations of these synthetic dura grafts are polytetrafluoroethyl (Hatanaka, 1992; Vinas et al., 1999; Grouls et al., 2000), polydiox (Vinas et al., 1999), hidrogel (Alleyene et al., 1998), hydroxy-ethyl-methacrylate-hydrogen (Bhatia et al., 1995), biosynthetic cellulose (Dietemann et al., 2005), Vicryl mesh (Nussbaum et al., 1989) and absorbable elastin fibrin material (San-Galli et al., 1996; Shimada et al., 2006). We can summarize the mechanisms of action as giving time to connective tissue for closing where they are applied up until absorbed (Aykan et al., 2002). Because of causing severe foreign body reaction, failure to create enough collagen production due to the higher amount of synthetic components in this first generation of synthetic dura grafts, more modern agents were developed. In recent years, the two agents; Beriplast P® (Dunn and Goa, 1999) and Tissudura® (Knopp et al., 2005; Cappabianca et al., 2006) have been popular in practice of neurosurgery (Handa and Koyama, 1989). Beriplast forms a waterproof barrier composed of tightly associated cells through connective tissue (Dunn and Goa, 1999; Eberhard et al., 2006). Tissudura is different from other collagen spongosts as it contains cross-links and therefore less CSF leak was reported (Esposito et al., 2008).

In our study, we compared the efficacy and side effects of these two products and assessed our findings in terms of the effects of dural grafts on brain tissue, bone tissue and epidural space. According to our results, Beriplast caused much more severe inflammation on cortex while this inflammation was mild in Tissudura group. When we compared Tissudura group

with the control group in terms of parenchymal edema and gliosis, the difference was not significant. On the other hand, we have found a significant increase in cortical parenchymal edema in Beriplast groups. So we can say that synthetic dural materials cause inflammation in cerebral cortex and some of them cause much cortex edema and gliosis. If we look at the inflammation in the epidural space; a slight increase in inflammation was detected by the Tissudura but this increase was much more severe in Beriplast group when we compared with sham.

In terms of bone foreign body reaction; a severe reaction was determined in Beriplast group.

When we look at the personal surgical observation in our study, a quite satisfactory and thick connective tissue, which had a tight connection with dura mater, was observed during the decapitation of Beriplast group. Severe inflammation and fibrosis that we found at histopathological evaluation in Beriplast group can explain this result.

According to the findings of our study, the last generation dural grafts result in different degrees of the reaction. Severe inflammatory reaction can provide more satisfactory results in terms of watertight dural closure but on the other hand, the same reaction can be a disadvantage to the surrounding tissue.

The repair of the dura water tightly with the least reaction has been the ideal target in neurosurgery but today; it seems difficult to catch this target in similar rate with even the most homogeneous, most modern dural grafts.

REFERENCES

- Alleyene, H., Cawley, C., Barrow, L., Poff, C., Powell, D., Amarpreet, B., 1998. Efficacy and biocompatibility of a photopolymerized, synthetic, absorbable hydrogel as a dural sealant in a canine Craniotomy model. *Journal of Neurosurgery* 88, 308-313.
- Ayhan, S., Tugay, C., Ortak, T., Prayson, R., Parker, M., Siemionow, M., Papay, F.A., 2002. Effect of bioabsorbable osseous fixation materials on Dura Mater and brain tissue. *Plastic and Reconstructive surgery* 109, 1333-1338.
- Bhatia, S., Bergethon, R., Kemper, T., Rosiello, A., Zimbardi, P., Franzblau, C., Spatz, E.L., 1995. A synthetic dural prosthesis constructed from hydroxyethylmethacrylate hydrogels. *Journal of neurosurgery* 83, 897-902.
- Cappabianca, P., Esposito, F., Cavallo, M., Messina, A., Solari, D., Somma, M., de Divitiis, E., 2006. Use of equine collagen foil as dura mater substitute in endoscopic endonasal transsphenoidal surgery. *Surgical Neurology* 65, 144-149.
- Chappell, E., Pare, L., Salehpour, M., Mathews, M., Middlehof, C., 2009. GORE PRECLUDE® MVP® dura substitute applied as a nonwatertight 'underlay' graft for craniotomies: product and technique evaluation. *Surgical Neurology* 71, 126-129.
- Dietemann, J., Bernardo, R., Bogorin, A., Eid, M., Koob, M., Nogueira, T., Vargas, M.I., Fakhoury, W., Zöllner, G., 2005. Normal and abnormal meningeal enhancement: MRI features. *Journal of Radiology* 86, 1659-1683.
- Dunn, J., Goa, L., 1999. Fibrin sealant: A review of its use in surgery and endoscopy. *Drugs* 58, 863-886.
- Eberhard, U., Broder, M., Witzke, G., 2006. Stability of Beriplast P fibrin sealant: storage and reconstitution. *Journal of Pharmacology* 313(1-2), 1-4.
- Esposito, F., Cappabianca, P., Fusco, M., Cavallo, L., Bani, G., Biroli, F., Sparano, A., de Divitiis, O., Signorelli, A., 2008. Collagen-only biomatrix as a novel dural substitute Examination of the efficacy, safety and outcome: Clinical experience on a series of 208 patients. *Clinical Neurology and Neurosurgery* 110, 343-351.

- Greenberg, S. 1994, Handbook of neurosurgery. Cerebrospinal fluid fistula. Third edition.
- Grouls, R., Korsten, E., Ackerman, E., Hellebrekers, L., Zundert, A., Breimer, D., 2000. Diffusion of n-butyl-p-aminobenzoate (BAB), lidocaine and bupivacaine through the human dura-arachnoid mater in vitro. *European Journal of Pharmaceutical Sciences* 12, 125-131.
- Handa, J., Koyama, T., 1989. Use of fibrin glue (Beriplast P) in neurosurgical practice. *Nippon Geka Hokan* 58, 231-235.
- Hatanaka, M., 1992. Expanded DPTFE surgical membrane for dura mater substitutes. *Research of New Medical Devices* 1, 183-193.
- Kelly, F., Oskouian, R., Fineman, I., 2001. Collagen Sponge Repair of Small Cerebrospinal Fluid Leaks Obviates Tissue Grafts and Cerebrospinal fluid diversion after pituitary surgery. *Neurosurgery*. 49, 885-890.
- Knopp, U., Christmann, F., Reusche, E., Sepehrnia, A., 2005. A new collagen biomatrix of equine origin versus a cadaveric dura graft for the repair of dural defects-a comparative animal experimental study. *Acta. Neurochirurgica*. 147, 877-887.
- Lage, J., Espejo, M., Palazon, J., Hernandez, F., Puerta, P., 2006. Autologous tissues for dural grafting in children: A report of 56 cases. *Childs Nervous System*. 22,139-144.
- Malliti, M., Page, P., Gury, C., Chomette, E., Nataf, F., Roux, F., 2004. Comparison Of Deep Wound Infection Rates Using A Synthetic Dural Substitute (Neuro-patch) or Pericranium Graft For Dural Closure: A Clinical Review Of 1 Year. *Neurosurgery*. 54, 599-604.
- Matsuoka, H., Yano, K., Katsuta, Y., Morita, M., Kounoe, S., Seo, Y., Saito, T., Tomoda, H., 1996. Advantages and safety of local treatment with MMC/Beriplast P for cancer tumors. *Cancer Chemotherapy & Pharmacology*. 38, 508-512.
- Mukai, T., Shirahama, N., Tominaga, B., Ohno, K., Koyama, Y., Takakuda, K., 2008. Development of watertight and bioabsorbable synthetic dural substitutes. *Artificial organs*. 32, 473-483.
- Narotam, P., Van Dellen, J., Bhoola, K., Raidoo, D., 1993. Experimental evaluation of collagen sponge as a dural graft. *British Journal of Neurosurgery* 7, 635-641.
- Narotam, P., Van Dellen, J., Bhoola, K., 1995. A Clinicopathological study of collagen sponge as a dural greft in neurosurgery. *Journal of Neurosurgery* 82, 406-412.
- Narotam, K., Jose, S., Nathoo, N., Taylon, C., Vora, Y. 2004, Collagen Matrix (DuraGen) in Dural Repair: Analysis of a New Modified Technique. *Spine*. Newyork: Lippincott Williams & Wilkins.
- Narotam, K., Qiao, F., Nathoo, N., 2009. Collagen matrix duraplasty for posterior fossa surgery: evaluation of surgical technique in 52 adult patients. *Journal of Neurosurgery* 111, 380-386.
- Nistor, F., Chiari, M., Maier, H., Hehl, K., 1997. The Fixed Combination of Collagen With Components of Fibrin Adhesive-A New Hemostyptic Agent in Skull Base Procedures. *Skull Base Surgery*. Thieme Medical Publishers, New York.
- Nussbaum, E., Maurer, K., McDonald, V., 1989. Vicryl (Polyglactin 910) mesh as a dural substitute in the presence of pia arachnoid injury. *Journal of Neurosurgery*. 71, 121-127.
- San-Galli, F., Deminiere, C., Guerin, J., Rabaud, M., 1996. Use of a biodegradable elastin-fibrin material, Neuroplast, as a dural substitute. *Biomaterials*. 17, 1081-1085.
- Schelling, G., Block, T., Gökel, M., 1998. Application of fibrinogen-trombin-collagen-based hemostatic agent in experimental injuries of liver and spleen. *Journal of Traumatology*. 28, 472-475.
- Sekhar, N., Sarma, S., Morita, A., 2001. Dural Reconstruction with Fascia, Titanium Mesh, and Bone Screws: Technical Note. *Neurosurgery*. 49, 749-752.
- Shimada, Y., Hongo, M., Miyakoshi, N., Sugawara, T., Kasukawa, Y., Ando, S., 2006. Dural substitute with polyglycolic acid mesh and fibrin glue for dural repair: Technical note and preliminary results. *Journal of Orthopaedic Science*. 11, 454-458.
- Stendel, R., Danne, M., Fiss, I., Klein, I., Schilling, A., Hammersen, S., 2008. Efficacy and safety of a collagen matrix for cranial and spinal dural reconstruction using different fixation techniques. *Journal of Neurosurgery*. 109, 215-221.
- Takçı, E., Kadioglu, H., Bağçeci, H., Aydın, İ., 2001. Deneysel Kranial Dural Defektlerin Onarımında Dehidrate Human Dura Mater Graftlerinin Kullanımı Histopatolojik Değerlendirme. *Türk Nörosirürji Dergisi*. 11, 178-184.
- Topsakal, C., Barut, S., Bilge, T., Sahin, Y., Altundal, N., Aydın, Y., 1993. Nöroşirürji'de Fibrin Yapıştırıcılarının kullanımı: 6 Olgunun Analizi. *Türk Nörosirürji Dergisi*. 3, 30-34.
- Vinas, F., Ferris, D., Kupsky, W., Dujovny, M., 1999. Evaluation of expanded polytetrafluoroethylene (ePTFE) versus polydioxanone (PDS) for the repair of dura mater defects. *Neurological Reseach*. 21, 262-268.

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