HISTOLOGICAL EVALUATION OF CORTICAL BONE REACTION TO PMMA CEMENT

by L. N. JENSEN, J. STÜRUP, M. KRAMHØFT and J. S. JENSEN

This study was designed to investigate histological changes in the tibia of adult mongrel dogs receiving PMMA bone cement in one tibial shaft and an inert filler, Bone wax®, in the other. Sixteen dogs were used, 2 dogs were investigated at one week, 6 dogs at four weeks and 8 dogs at twelve weeks. It was shown in this study, that intramedullary implantation of PMMA bone cement leads to considerable impairment of bone remodelling. At each period of observation the index periosteal apposition/cortex thickness was lower on the cemented side ; at 4 weeks an index of 0.42 (0.17-0.64) compared to 0.72 (0.42-0.91), and a 60-70 µm concentric fibrillar fibrous membrane was seen between cement and bone. On the Bone wax® side few or no areas of fibrous tissue were detected at both 4 and 12 weeks ; and when such tissue was present, islands of bone developing directly onto the wax was seen. The bone remodelling was impaired on the cemented side and limited to the outer half after 4 weeks.

Keywords : bone cement ; bone wax ; bone remodelling ; fibrous membrane ; canine histology.
Mots-clés : ciment ; cire ; remaniement de l'os ; membrane fibreuse ; histologie chez le chien.

RÉSUMÉ

L. N. JENSEN, J. STÜRUP, M. KRAMHØFT et J. S. LENSEN. Évaluation histologique de la réaction de l'os cortical au contact du ciment PMMA.

Cette étude a été entreprise en vue de rechercher les modifications histologiques chez des chiens adultes dont la cavité médullaire d'un tibia a été bourrée de ciment PMMA et, celle du tibia opposé, de cire chirurgicale (Bone wax®).
Seize chiens ont été utilisés, deux à l'échéance d'une semaine, six à quatre semaines et huit à douze semaines. Il a été démontré que l'implantation du ciment détermine une dégradation importante du remaniement osseux. À chaque période d'observation, l'index d'apposition osseux périostique par rapport à l'épaisseur corticale est inférieur du côté ayant reçu du ciment. Une membrane fibreuse d'une épaisseur de 60 à 70 microns s'est constituée entre le ciment et l'os.
Au côté ayant reçu de la cire chirurgicale, il n'y a pas ou guère de tissu fibreux à l'échéance de 4 et 12 semaines et, lorsque ce tissu est présent, on observe la formation d'ilôts osseux au contact de la cire. Le remaniement osseux est altéré du côté ayant reçu du ciment. Il est réduit à la périphérie à l'échéance de 4 semaines.

SAMENVATTING

L. N. JENSEN, J. STÜRUP, M. KRAMHØFT en J. S. LENSEN. Histologische evaluatie van de reactie van corticaal bot versus PMMA cement.

Deze studie werd opgezet om de histologische veranderingen te onderzoeken in de tibiae van volwassen bastaardhonden, waarbij PMMA botcement in één tibiaschaft werd ingebracht en een inerte vulling, Bone-wax®, in de andere.
Zestien honden werden gebruikt. Twee werden onderzocht na één week, zes na vier weken en acht na twaalf weken.
In deze studie werd aangetoond dat intramedullaire inplanting van PMMA botcement tot een aanzienlijke ontregeling van de botombouw leidt.
In iedere observatieperiode was de index periostale aanmaak/cortexdikte lager aan de gecementeerde

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zijde. Op vier weken bedroeg de index 0.42(0.17-0.64) in vergelijking met de normale 0.72 (0.42-0.91). Een concentrisch fibrillair fibreus membraan van 60-70 µm dikte werd geobserveerd tussen cement en bot. Aan de Bone-wax® zijde werden weinig zones van fibreuze membraanvorming aangetroffen, noch op vier noch op twaalf weken.
Indien toch aanwezig ging dit gepaard met vorming van boteilandjes vlak tegen de was.
Aan de cementzijde was de botombouw na vier weken beperkt tot de buitenste helft.

INTRODUCTION

A necrotic bone layer of 0.5 to 0.8-mm thickness in direct proximity to acrylic polymethylmethacrylate (PMMA) bone cement has been reported in human studies of joint implants 2 to 3 weeks after implantation (2, 21). In animal studies, the bone necrosis has included about 1/2 to 2/3 of the endosteal side of the cortex, following reaming, suction and intramedullary filling with bone cement (5, 18).
The aim of our study was to examine histologically the bone reaction to intramedullary filling with acrylic cement on one side and inert bone wax (7, 19) on the contralateral side, after identical surgical preparation of both sides.

MATERIALS AND METHODS

Sixteen adult mongrel dogs (weight 20 to 30 kg) were followed for 1 week (2 animals), 4 weeks (6 animals) and 12 weeks (8 animals). With the animal under general anesthesia a longitudinal incision was made through the patellar ligament, and the tibia was reamed with hand-driven reamers to a diameter of 8 to 9 mm. The cavity was curetted, brushed, and flushed with saline. A suction tube was applied distally and the medullary cavity filled with a cement gun from the distal end with a radiopaque acrylic bone cement (Palacos®) after normal mixing on one side and with Bone wax®, (Ethicon), made radiopaque by adding 15% by weight zirconium oxide, on the contralateral side. The wax was first heated to 40°C to make it soft enough to inject with a cement gun. Pressurization was applied bilaterally with a hand tool until the component was stiff. Postoperatively radiographs were taken to verify adequate filling. One gram intravenous ampicillin was given prophylactically for 3 days. All dogs recovered quickly from surgery and showed no signs of infection or lameness.
On sacrifice both tibias were harvested. Two transverse and two longitudinal segments were manually cut from the middiaphysis. The blocks were immersed in 10% buffered formalin solution for 3 weeks and then dehydrated with ethanol. The undecalcified bone was embedded in epoxy resin, and sections of 50 to 100-µm thickness were sliced with an Exact® cutting and grinding system (Norderstedt, W. Germany). The sections were stained with van Gieson picro-fuchsin/Stevenels blue or a modified hematoxylin-eosin stain (8, 14). Besides an ordinary histological examination, measurements of the thickness of the periosteal apposition and the cortex were made along nine randomly selected radians at 25 times magnification.. To compensate for inegality in preparation of the sections a periosteum cortex ratio was calculated for each set of records. The median values were statistically analyzed by Wilcoxon rank sum test.

RESULTS

The histological examination included three areas : the periosteal, the cortical and the endosteal (bone-cement interface) reactions.

OBSERVATION PERIOD 1 WEEK

A periosteal bone apposition of immature radially-orientated trabeculae, was observed bilaterally, but it was more prominent after implantation with bone wax as compared with the cement (table I). In the Bone wax® group the cortical necrosis was less extensive and limited to one-third of the endosteal cortex. In the cemented group more than two-thirds of the endosteal cortex showed signs of bone necrosis with empty osteocyte lacunae. Only in the outer cortex were vital osteocytes demonstrated. A membrane of approximately

40 µm was observed in the cement-bone interface. This membrane was amorphous and composed of bone-marrow elements. Bone fragments and debris from reaming were also observed in the interface. The same features were seen at the wax-bone interface on the contralateral side.

OBSERVATION PERIOD 4 WEEKS

The periosteal apposition had markedly increased in thickness in both groups. Among 6 dogs 5 showed thicker periosteal apposition in the bone-wax group than in the cemented (table I). A distinct line of demarcation was observed between the dead cortex and the new periosteal apposition (fig. 1).

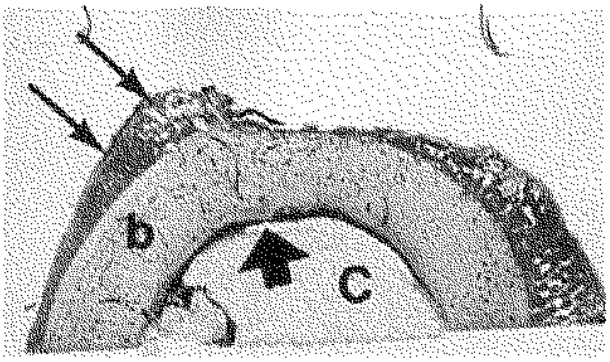

Fig. 1A

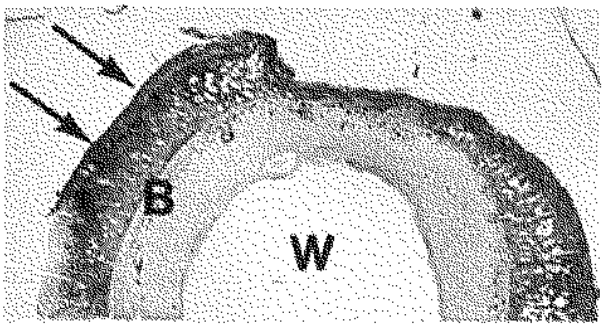

Fig. 1B

Fig. 1. — Transverse sections of canine tibias 4 weeks after intramedullary filling with acrylic bone cement or with Bone wax®, stained with van Gieson picro-fuchsin/Stevenels blue.
A. Periosteal apposition (arrows) is moderate. Cement (C) and bone (B) are separated by a fibrous membrane (thick arrow) (× 1).
B. In the Bone wax® group the periosteal apposition is thicker (arrows). No fibrous membrane is seen between bone (B) and wax (w) (dissolved during preparation) (× 1).

New osteons of vital tissues had formed in the necrotic cortical bone. The osteoid bone formation was more prominent in the Bone wax® group and scattered throughout the whole cortex. On the cemented side it was limited to the outer half of the cortex. No particular osteoclastic activity was noted in the cortex on either side.
The wax-bone interface showed a 40-µm amorphous membrane, but at most sites new bone had been formed at the endosteal surface. A fibrous membrane of 60-70 µm, however, containing circulary oriented fibrils was observed at the cemented interface. In a few places this membrane was interrupted by small islands of osteoid bone with direct apposition to the cement (fig. 2).

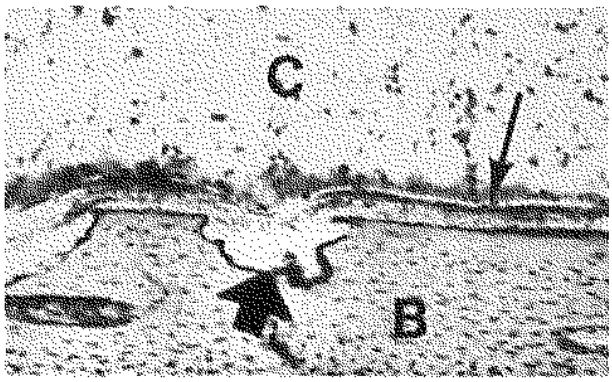

Fig. 2A

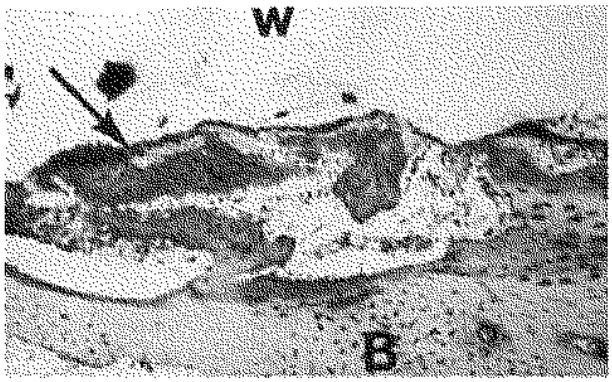

Fig. 2B

Fig. 2. — Four weeks after implantation.
A. Histologic section, stained with van Gieson picro-fuchsin/Stevenels blue showing acrylic cement in situ (C) and bone (B) separated by a fibrous membrane (thin arrow). An active osteoclastic zone is seen (thick arrow) (× 100).
B. Osteoid bone with osteoblasts (thin arrow)adjacent to bone wax (w). Old cortex (B). Stained with van Gieson picro-fuchsin/Stevenels blue (× 100).

Table I

Follow-up Period (Wks)	bone wax®			bone cement		
	Apposition	Cortex	Index	Apposition	Cortex	Index
1 (N = 2)	100 (0-475)	3500 (2750-4000)	0.03 (0-0.16)	0 (0-125)	3500 (2500-4000)	0.00 (0-0.4)
4 (n = 6)	2000 (0-3500)	3000 (2000-4500)	0.72 (0.42-0.91)	1250 (0-2500)	3000 (1750-4000)	0.42 (0.17-0.64)
12 (N = 8)	1750 (500-5750)	3000 (2000-4000)	0.62 (0.5-1.0)	1000 (0-4000)	3000 (1250-3750)	0.38 (0.15-0.83)

Median values (Range) of periosteal apposition and cortical thickness (μm).
Index = Periosteum/cortex ratio.

OBSERVATION PERIOD 12 WEEKS

No further periosteal apposition was seen from the 4th to the 12th week, but the reaction remained thicker in the Bone wax® group ($p < 0.039$) (table I). Resorption lacunae were now clearly visible in the zone between old cortex and the new periosteal apposition, effacing the demarcation, especially on the wax side. Active remodelling of the entire cortex was observed in both groups but it was less prominent on the cemented side. The endosteal bone formation had increased in thickness from the 4th to the 12th week.

At 12 weeks an amorphous membrane with few or no areas of fibrous tissue and patches of direct bone apposition was still observed on the Bone wax® side. At the cement-bone interface a fibrous membrane of 60 to 70 μm, containing circularly oriented fibrils and few cells was seen. Furthermore loose connective tissue with plasma cells and lymphocytic infiltration and direct bone-to-cement contact was found.

DISCUSSION

Previous comparative studies on the bone reaction to acrylic bone cement have used reamed but unfilled tubular bone as a control (4, 5, 12, 18, 20), or have inserted into the medullary cavity an acrylic rod (5).

We have tried to eliminate methodological errors by preparing the medullary cavities in an identical fashion, but we used an inert filler, bone wax® (7, 19), on the control side. Potential local toxicity of the radiopaque dye was avoided by adding a similar 15% by weight concentration of zirconium oxide, and any influence of mechanical stress was avoided by simply filling the medullary cavity without applying any implant.

The present model is thus influenced by the effect on bone vascularity by reaming, brushing and suction (4, 5, 18), and the bone marrow circulation is interrupted by plugging the medullary cavity on both sides.

It has been claimed that the bone necrosis following intramedullary cementation with acrylics might be caused by the high exothermia (5, 12, 17) or from leaking toxic monomer or aromatic amines during polymerization (9, 10, 12, 16). This study did not enable us to distinguish between causative factors, but did disclose their combined effects.

The initial cortical necrosis was much more prominent on the cemented side, indicating that factors other than disruption of the circulation are of importance. Also the remodelling of dead cortical bone was phase-shifted, being delayed on the cemented side.

We did not find a direct relationship between the amount of bone necrosis and the periosteal apposition, as was previously reported in rabbits (5). Our attempt at partial quantification of the histology was rather successful. In accordance with Malefijt *et al.* (13) we found an earlier and much

more prominent periosteal apposition and less bone necrosis on the side not plugged with acrylics. We do not agree that this phenomenon is caused by mechanical factors (13), as both tubular bones were treated identically. It has been suggested that the bone remodelling appears from the periosteal layer and outer cortex (1, 18). This seems feasible from our study, but it also seems probable that heat generation and release of toxic chemical components inhibits the regeneration potential of the periosteum.

Membrane formation at the cement-bone interface has previously been described in humans (2, 6), and in animal experiments (15, 18, 21, 22). The membrane has been classified as similar to synovial tissue (3, 6, 22), or as a thin fibrous layer (2, 18, 21). We can not rule out differences in interpretation of the histology, but agree that an obvious membrane is formed at the cement-bone interface, and to lesser extent at the wax-bone interface. In accordance with others (11, 15) we did, however, observe direct approximation of new bone to cement or to Bone wax®, although it was again phase-shifted.

In conclusion, we found that acrylic bone cement seriously influenced the viability of cortical bone and its remodelling as compared to inert Bone wax®. Whether this results from high exothermia or release of toxic chemical constituents is still unknown. Furthermore initial membrane formation at the cement-bone interface might be a predecessor of prosthetic loosening.

Investigations after 4 weeks seem to offer the most information in canine experiments. With the limited access to animals for experimental investigations a 4-week model should be used for screening purposes.

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