White Paper 5 – BoneWelding® Implants transform into bone after resorption

Background and introduction

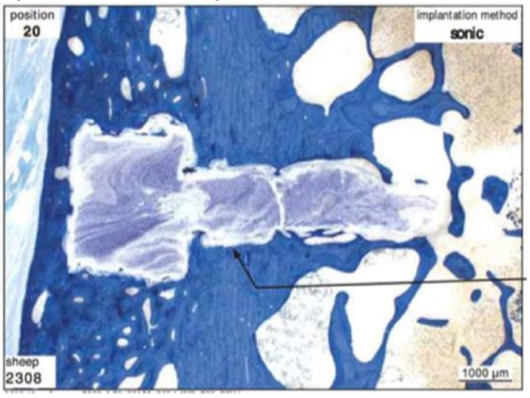
The BoneWelding® Technology is a revolutionizing fixation technique that uses ultrasonic energy to anchor a polymer implant into bone. The polymer infiltrates the small cavities in the surrounding cancellous bone by local melting at the implant's surface. This paper is the fifth in the VetWelding white paper series about PLDLLA BoneWelding® implants and their different degradation phases in small animals and investigates the bone remodeling after degradation.
Bone remodeling can be divided into two main phases; the first remodeling phase starts 2-3 months after implantation in the implant's close vicinity. The second phase occurs after complete resorption of the polymer when new bone fills the previously occupied spaces. For the second phase to occur, the polymer needs to be completely resorbed.

In a clinical study of the Weldix Anchor® in humans, it was observed that after 30 - 48 months, the anchor was not yet completely resorbed but that the interface between bone and anchor had been remodeled without any signs of osteolysis[1]. Further studies with ultrasonically inserted PLDLLA pins in humans reported new bone formation [2] and partial to fully remodeled bone after four years in most patients [3]. The human studies can be used as a first indication for the expected bone remodeling activity in dogs, as the remodeling in dogs is reported to be generally faster than in humans [4, 5].

Bone remodeling around implants inserted by BoneWelding® Technology

Langhoff investigated the bone remodeling and advanced to complete polymer resorption after insertion of pins using BoneWelding® Technology and, as a control, polymer press-fitted pins from the same material. The investigated pins were both resorbable, one a PLDLLA Resomer® LR708 (Evonik Röhm GmbH, Darmstadt, Germany) and one a faster resorbing PDLLA Resomer® R208 (Evonik Röhm GmbH, Darmstadt, Germany). *Figure 1* shows histologies of both polymers after one year. The faster degrading implant (PDLLA) (*Figure 1*, right) is completely resorbed after one year, and the cavity is filled with new trabecular bone [6]. The slower resorbing material (*Figure 1*, left) shows clear signs of advanced degradation and disintegration. Histologically, there are no signs of fibrous capsule formation caused by pronounced inflammatory reaction nor osteolysis around the implant; on the contrary, bone density was found to be increased slightly though not significantly around the implant. The histological situation regarding remodeling, degree of degradation, and bone replacement is identical to the mechanically inserted reference implants (*Figure 2*).

BoneWelding® Pin of PLDLLA
(Weldix® Anchor)



Bone Welding® Pin of PDLLA
(Resorb Pin and Plate System)

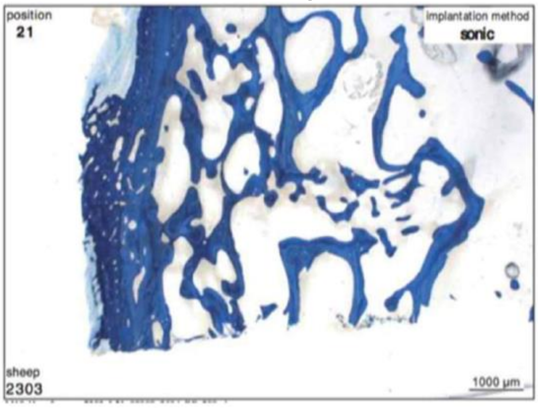


Figure 1: Polymer pin implants, ultrasonically inserted by Bone Welding® at 12 months after implantation. Both implants show ongoing (Left: PLDLLA, Resomer® LR 708) or complete (Right: PDLLA, Resomer® R208) resorption and replacement by new bone, no signs of bone lysis or of fibrous membrane formation [6].

Press-fitted Pin of PLDLLA (Control) | Press-fitted Pin of PDLLA (Control)

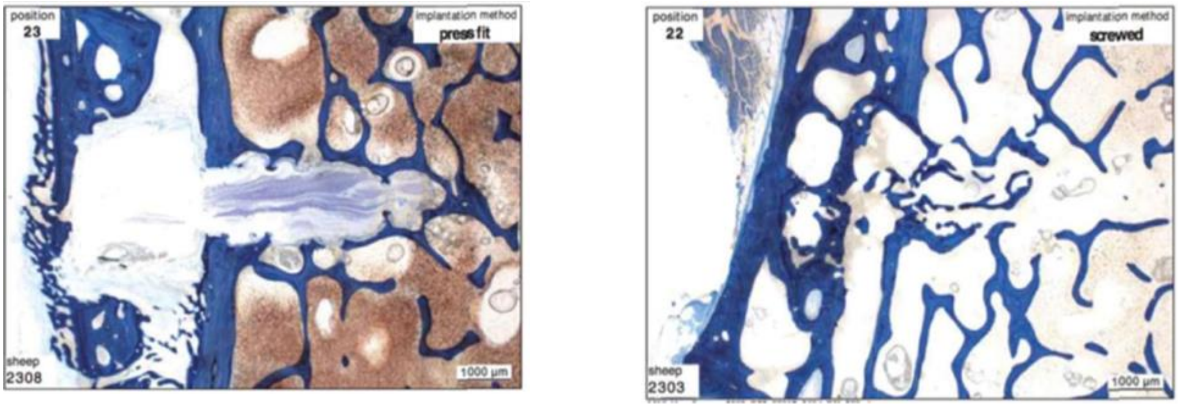


Figure 2: Polymer pin implants, mechanically inserted at 12 months after implantation. Both implants show ongoing (Left: PLDLLA, LR 708) or complete (Right: PDLLA, R208) resorption and replacement by new bone [6].

In the same study, titanium implants, partially coated by PLDLLA or PDLLA, were implanted in the pelvis and subjected to load through contractions of the gluteus maximus muscle. Uncoated titanium implants were used as control. In addition to the histological analysis, all implants were characterized biomechanically and histomorphometrically. Both methods showed that bone formation and osseointegration (measured by bone-implant contact) were faster and more effective for the coated implants inserted by BoneWelding® Technology [6]. During the first three months, the increase of new bone contact with the implant as well as the increase in anchoring strength was significantly faster and higher than with the uncoated control, and even though bone-implant leveled out after 12 months, the mechanical stability remained to be higher (see *Figure 3*). Although the PDLLA degrades faster, there was no difference in strength between the PDLLA and the PLDLLA coated titanium implants measured by torque out. The histological reactions of the polymer-coated implants were comparable to those of pins discussed above: the R208 coating transformed into bone completely, while the slower degrading LR708 was still present but in an advanced state of degradation. Furthermore, it was shown that the degradation and resorption of the polymer did not hamper the osseointegration of the titanium implants. On the contrary, the enhanced primary stability provided by the polymer coating accelerated osseointegration significantly, as indicated by the considerably higher bone-implant contact values.

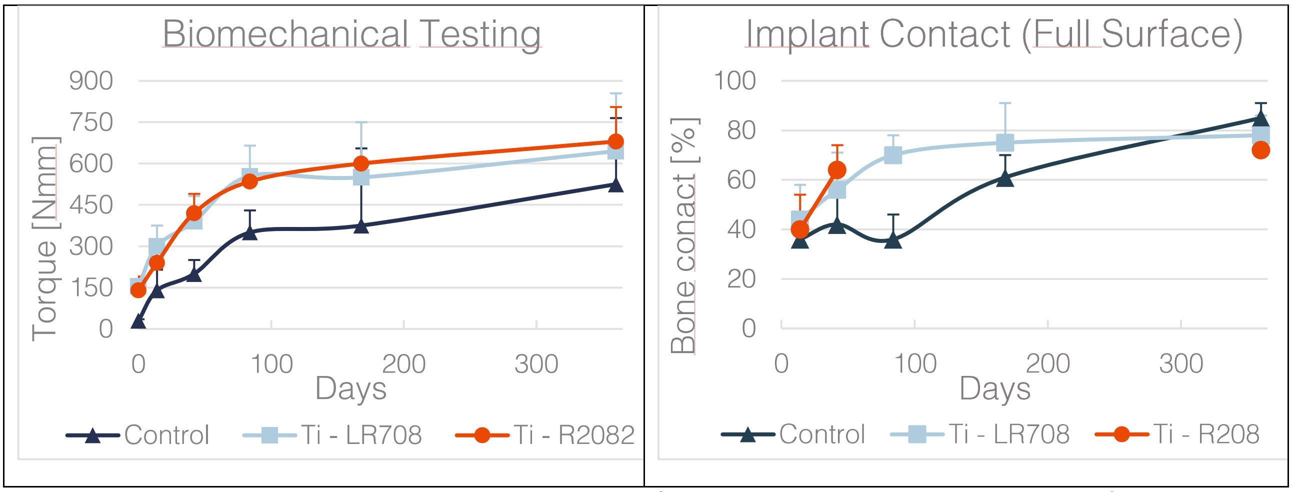


Figure 3: Comparison between the faster resorbing Resomer® R208 and the slower resorbing Resomer® LR708 regarding mechanical stability (left) and bone-implant contact (right). The higher resorption rate does not have a negative impact on torque-out strength nor the bone-implant contact area [6].

The above findings correlate to an earlier study investigating acute inflammatory reactions (2 months) and bone remodeling (6 months) around ultrasonically inserted PLDLLA pins and partially coated titanium

implants. The implants were implanted into sheep's distal femur and proximal tibia, addressing the histological reaction in cancellous and cortical bone, specifically [7].
In addition to the sheep studies, a comparative study in rabbits was performed to evaluate the influence of ultrasonically implanted biodegradable pins compared to press-fitted pins. It was concluded that ultrasound-aided implanted pins show significantly better bone-implant contact than the press-fitted ones [8]. Hence, these results indicate ultrasonically applied biodegradable polymers could provide better stability, enhance and accelerate osseointegration and prevent current problems with biodegradable implants such as implant migration or micromotion.

Discussion

A literature review was conducted to find a correlation between bone remodeling or osteolysis to material and degradation properties of PLDLLA implants. Material-related bone growth or inhibition was observed in different implant designs and indications. Hence pin and cage studies were considered to show the impact on the ability of new bone formation in the presence of degrading PLDLLA. Comparisons between PLDLLA and titanium implants generally show equal or better bone growth properties for the PLDLLA material. *Kääb et al.* investigated the bone attachment and osteoconductivity to a suture anchor made of PLDLLA or titanium in a sheep study. They observed no signs of osteolytic activity for either of the two materials.

Additionally, they observed that the suture hole in the polymer implant was fully bridged compared to only partially bridged in the titanium anchor. The authors demonstrated that the PLDLLA anchor is superior to the titanium implant regarding osteoconductive properties. They concluded that PLDLLA implants could be used safely as an alternative to titanium implants [9]. Studies on PLDLLA pins in sheep osteotomies showed bone healing after three months and bony replacement or connective tissue after 36 months in the spaces occupied by the polymer before [10]. Another study reports complete bone healing after three months and a slight dilation of the pin canal between 12 and 18 months, which disappears after 36 months [11].

In conclusion, the presence of degrading PLDLLA does not prevent the bone from growing. Furthermore, it was observed that **ultrasonically applied pins could enhance stability by increasing bone-implant contact**. Test results of a faster resorbing but otherwise identical polymer pin made out of PDLLA (Resorb Pin and Plates) showed complete **resorption and replacement of the drill hole by new bone** after one year. The behavior with the slower resorbing PLDLLA (Weldix® Anchor) is expected to be the same but requires rather two years than one. Studies on **ultrasonically applied pins in humans** showed **promising remodeling activity**, which is expected to be even **better in canines** due to the **faster canine bone remodeling**.

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