Bone-Forming Effect of a Static Magnetic Field in Rabbit Femurs

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This study investigated the level of magnetic energy around implants possessing a static magnetic field (SMF) and assessed the in vivo influence of SMF on bone regeneration. Implants possessing a sintered neodymium magnet internally were placed in a rabbit femur. An implant without SMF was placed as control. After 12 weeks of healing in vivo, the bone samples were subjected to histologic/histomorphometric evaluation. The bone-to-implant contact for the test group and the control group were 32.4 ± 13.6% and 17.1 ± 4.5%, respectively, and the differences were statistically significant (P < .05). The results suggested that the SMF promoted new bone apposition.


Recently, the use of magnetic forces has been shown to present bone regenerative properties.1,2 Magnetic forces can be classified in two types, variable magnetic fields (VMFs) in which strength and direction alter with time, and static magnetic fields (SMFs) where magnetically constant fields are generated.

The pulsed electromagnetic field is a type of VMF that is known to enhance bone regeneration in vitro and in vivo,3,4 and it has been applied in orthopedic surgery to treat bone fractures.5 It also has shown regenerative effects on the mandibular fracture healing process.6 Furthermore, some studies have even shown that the effect of pulsed electromagnetic fields enhances osseointegration to dental implants.7

Although magnetic treatment is promising, some drawbacks have been indicated that prevents it from being widely introduced in clinical practice. For example, the cost-effectiveness of the therapeutic device has been questioned. A large electromagnetic wave pulse emission device is necessary to provide the treatment with VMFs, and patients require multiple magnetic treatments, which is an economic and physical burden on them.8 Moreover, the VMFs cannot be applied to patients having certain implantable medical devices, such as cardiac pacemakers, which restricts...
their indication. Therefore, the application of SMFs, which requires no specific external device, has recently attracted attention. The SMFs also have been reported to be effective in regeneration of the bone.\textsuperscript{1,9} In many cases, the implanted medical device that contraindicates the use of VMFs itself possesses an SMF that stimulates osteogenesis by promoting osteoblastic differentiation,\textsuperscript{10–13} which is mainly attributed to activation of p38 phosphorylation.\textsuperscript{14,15}

Although further evidence is necessary, SMFs may present a solution in implant dentistry, since different types of implantable devices are used during surgery intended for bone regeneration. Devices such as occlusal membranes, dental implants, and healing abutments require osteoconductive or osteointegrative properties to function in an effective manner.\textsuperscript{16} Since SMFs supposedly stimulate osteogenesis, development of metallic devices that would enhance and stimulate osseointegration would be of significant interest.

Based on these considerations, the aim of the present study was to investigate the level of magnetic energy around cylindrical implants possessing SMFs and to assess the in vivo influence of SMFs on osseointegration around them when placed in the rabbit femur diaphysis. The level of bone regeneration was measured by means of histologic/histomorphometric evaluations.

Materials and Methods

Specimen Preparation

The test specimens consisted of a large-body nonmagnetic stainless steel case, a small-body titanium case (titanium purity 99.485%), a neodymium sintered magnet, and a magnetic body with an umbo shape (Fig 1). By combining these components, implants with an SMF were made. The stainless steel case was used instead of the magnet as control.

The manufacturing process flow of the implants with SMF is presented in Fig 2. In brief, the large and small body titanium cases and magnetic umbo were manufactured using a cutting method. Thereafter, a neodymium sintered magnet was demagnetized and inserted into the large-body nonmagnetic stainless steel case (Fig 2a), followed by pressing the umbo to enclose the magnet (Fig 2b). At this point, laser welding was performed at the boundary between the disk covering the surface and the yoke of the magnet to prevent corrosion (Fig 2c). In the penultimate stage, the umbo was pressed into the small-body titanium case. Finally, the magnetic substance inside the specimen was magnetized again in a vertical direction after cleaning. The structure and dimension of the specimen used is illustrated in Fig 2d.
Magnetic Flux Distribution Measurement of Specimen Surface

To measure the magnetic flux distribution of specimens with SMF, measurement points were determined as presented in Fig 3. A Gauss meter (Model 4048, F.W. Bell) was used to measure the magnetic flux of each measurement points five times, and the average value was calculated.

Animal Preparation

Six New Zealand white rabbits (mean body weight 3.9 kg; range 3.3 to 4.5 kg) were used in the present study. The study was approved by the Ethics Committee for Animal Research at the École Nationale Vétérinaire d’Alfort (Maisons-Alfort, Val-de-Marne, France). All surgical procedures were performed under general anesthesia. The preanesthetic procedure comprised intramuscular administration of atropine sulfate (0.044 mg/kg) and xylazine chlorate (8 mg/kg). General anesthesia was then obtained following an intramuscular injection of ketamine chlorate (15 mg/kg). Thereafter, the hind legs were shaved and disinfected with iodine solution. After anesthetic and disinfection procedures, the proximal femur on each side was exposed and a 3-mm osteotomy was prepared on both sides for placement of implants (Fig 4). After placement of the specimens, the periostium was sutured separately using Vicryl 4-0 continuous suturing.

Histologic Preparation and Analyses

After 12 weeks of healing, the animals were euthanized with anesthesia overdose and the bone-implant specimens were removed en bloc. Thereafter, the specimens were placed in 4% paraformaldehyde for 24 hours. After fixation, the samples were rinsed in running tap water and subjected to dehydration in a series.

Fig 3  Dimension and measurement points of the specimens.

Fig 4  Surgical procedures. (a) Defects of 3 mm were created in the rabbit proximal femur. (b) Specimens were inserted into the defect.
of ethanol concentrations (70% to 100%) and infiltration in resin (concentrations from 30% to 100%) under constant vacuuming. They were then embedded in light-curing resin (Technovit 7200 VLC, Heraeus Kulzer). The embedded resin blocks were subjected to nondecalcified cutting-grinding sectioning. In brief, a central section of each sample was prepared using EXAKT cutting and grinding equipment to a final thickness of 20 µm. After polishing to exclude scratches, the sections were finally stained with a solution of toluidine blue and pyronin G.

Histologic analyses were performed using a light microscope (Eclipse ME600, Nikon), and the histomorphologic data was analyzed with image analysis software (Image J version 1.43u, National Institutes of Health). Calculation of bone-to-implant contact (BIC) ratio along the specimen surfaces was made using ×10 magnification objective. Histology and histomorphometry were both conducted in a blind manner.

### Statistical Analysis

The results from the histomorphometric measurements were expressed as means and standard deviations. The treatment groups were compared using Kruskal-Wallis test with the significance level set at $P \leq .05$.

### Results

#### Magnetic Flux

Table 1 shows the magnetic flux at each measurement point as indicated in Fig 3. The mean flux of magnetic force at points 1, 2, 3, and 4 were 43, 44, 53, and 162 mT, respectively. No significant difference was observed among specimens with respect to the magnetic flux.

#### Clinical Observation

Healing took place uneventfully without signs of infection. None of the implants were lost during the healing period, and all implants were clinically stable at the time of sample retrieval.

#### Histology and Histomorphometry

The representative histologic micrographs are presented in Fig 5. Newly formed bone (stained in deep purple) can be seen in close contact with the implant surface for both groups. No adverse biologic reactions were noted for either group. The corresponding histomorphometric BIC for the test and control group at 12 weeks after implant placement were 32.4 ± 13.6% and 17.1 ± 4.5%, respectively (Fig 6). BIC to the implant surface was statistically significantly higher for the implants with SMFs (test group, $P < .05$).
Discussion

The present study investigated the effect of metallic implants possessing SMF on bone regeneration in a rabbit femur model. A time point of 12 weeks was selected due to the fact that the implant surfaces were very smooth, requiring longer healing periods. It is well known that surface roughness plays an important role in acceleration of the osseointegration process. It has been suggested that a suitable surface roughness to obtain good bone conductivity is a moderately roughened implant surface with an average height deviation from a mean plane of 1 to 1.5 µm. However, the specimens in this study have smooth surfaces due to the manufacturing process. An implant surface that can obtain good bone response should be considered for future study.

The effect of the magnetic flux seemed to increase and was strongest at 12 weeks. The results showed that after 12 weeks in vivo, significantly enhanced osseointegration was achieved for the implants possessing SMFs compared to the control group without magnetic fields. The BIC percentage after 12 weeks for the control group was in line with previous studies investigating the degree of osseointegration. With regard to the macrogeometry of the tested implants, a cylindrical type was used to evaluate only the bone-implant interaction in a model where the effect of implant geometry can be excluded.

The positive osteogenic outcomes obtained in the current study are in accordance with a microCT analysis conducted by Kim et al showing an effect on bone regeneration around implants with 15 mT neodymium magnets located inside of the fixture. In a randomized controlled clinical trial, Siadat et al reported that immediately placed implants in fresh extraction sockets connected to healing abutments possessing SMF induced higher implant stability as measured by resonance frequency analysis, and less marginal bone loss at the early stages of bone healing (1 and 2 months).

Although the implanted metallic devices as presented in the current study represent a promising technology to promote osseointegration, clinical application should be thoroughly considered. Indication for permanent use should be avoided as much as possible until sufficient evidence is established. Interim applications intended for future removal of the implantable devices should be considered as an indication. Applications of a magnetic device as a part of dental implant components, such as cover screws, healing abutments, or fixation screws for block grafting, or occlusal membranes for space maintenance could significantly improve bone regeneration and integration.

Since the present study tested the bone regeneration properties at 12 weeks, future studies investigating shorter and longer periods are warranted to better understand biologic responses to devices possessing SMFs. The long-term effects of the magnetic field have yet to be confirmed, which means the bio-safety aspect must be determined before clinical trials are performed.

Conclusions

The present study revealed that SMFs generated by implants with neodymium magnet showed a significantly higher degree of BIC than a control group at 12 weeks in vivo.

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The authors declare no conflicts of interest.

References


