Prospective longitudinal outcome study assessing the use of BonAlive bioactive glass for attaining eradication of osteomyelitis and stimulation of bone healing in patients requiring surgery in osteomyelitic bone defects.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON46331

Source
ToetsingOnline

Brief title
BonAlive HRpQCT study

Condition

- Bacterial infectious disorders
- Bone disorders (excl congenital and fractures)
- Bone and joint therapeutic procedures

Synonym
bone infection; osteomyelitis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,BonAlive Turku, Finland

Intervention

Keyword: bioactive glass, HRpQCT, infection, osteomyelitis

Outcome measures

Primary outcome

First objective of this study is assessment of bone healing capacity of Bonalive bioactive glass by High Resolution peripheral Quantitative Computed Tomography (HRpQCT). Several bone parameters will be calculated during longitudinal follow up (see section 5.1).

Secondary outcome

Second objective of this study is the evaluation of bone strength based upon micro-finite element analysis (µFEA), calculated after HR-pQCT imaging. Bone strength will be evaluated using longitudinal µFEA outcomes of patients during follow up.

Third objective of this study is to assess the improvement of patient related outcomes assessed at 6, 52 and 104 weeks after surgery. This is an addition to the patient satisfaction obtained in standard follow-up algorithm of chronic osteomyelitis treatment.

Fourth objective of this study is to evaluate the infection eradication success of osteomyelitic bone defects reconstructed with BonAlive bioactive glass. This is an important outcome because the presence of an infection may influence the results of the HRpQCT scans, which makes these results no longer reliable. Absence of infection will be based upon clinical data, X-ray analysis and infection rates assessed in blood sample analysis, which belong to the standard follow-up algorithm of chronic osteomyelitis treatment.

Study description

Background summary

Osteomyelitis is the inflammatory process of bone combined with bone destruction generally caused by bacteria. These bony infections can be localized solely in bone, but they can also involve environmental tissues such as the bone marrow, periosteum and soft tissues. Osteomyelitis is commonly caused by a local spread of contiguous infections i.e. trauma or joint replacement, secondary to vascular insufficiency in patients with diabetes or due to a less common haematogenous spread of bacteria. Pathogenic micro-organisms causing these osteomyelitic infections are usually the Staphylococcus aureus bacteria, which can lead to acute or chronic osteomyelitis. Acute osteomyelitis usually develops and reduces in several days or weeks and can become chronic osteomyelitis, which is a long-lasting infection that can last for several months to even years.
Treatment of acute osteomyelitis with adequate systemic single-agent antibiotics is usually sufficient, where the treatment algorithm of chronic osteomyelitis generally consists of surgical debridement of the affected tissue and administration of local and systemic antibiotics. Debridement surgery and local antibiotic therapy are necessary because patients with chronic osteomyelitis have infected dead bone combined with poor local vascularisation, which lead to eradication difficulties when treated with solely systemic antibiotics (6). Regarding the local administration of anti-bacterial bone graft substitutes, such as antibiotic-loaded calcium sulphates or bioactive glasses, major developments are seen in the last few years.
A promising biomaterial used in the application of local eradication of infection is BonAlive bioactive glass (9, 10), Thereby BonAlive bioactive glass has excellent bone filling capacities for bone defects existing after debridement surgery. BonAlive is a S53P4 bioactive glass consisting of 53%

SiO2, 4% P2O5, 23% Na2O and 20% CaO produced by BonAlive Biomaterials Ltd in Finland. Due to this composition BonAlive is biodegradable, stimulates bone formation and has antibacterial effects that should lead to eradication of infection and bone healing when combined with debridement surgery in the treatment of chronic osteomyelitis.
Despite the fact that several studies stated good bone healing over several years after implantation of BonAlive bioactive glass, these conclusions were only established using the conventional radiology techniques. These studies assessed degradation of BonAlive based on a subjective estimation of the visibility of BonAlive particles on plain radiographic images. Imaging techniques such as plain radiographic imaging and computed tomography (CT) are not suitable for a reliable measurement of bony fusion of the implanted biomaterials because a lack of objective parameters related to bone growth or biomaterial degradation. To establish this bony fusion, high-resolution imaging should be advantageous, which can be performed using the High Resolution peripheral Quantitative Computed Tomography (HR-pQCT) imaging. HR-pQCT is an imaging technique based on the possibility of providing 3-dimensional images using computed tomography of the peripheral bone structures. Due to this high resolution we can assess bone density and bone architecture like trabecular and cortical bone structures up to a resolution of 82 µm. Thereby, using HR-pQCT enables the possibility to calculate some biomedical properties of bones, such as bone strength, using micro-finite element analysis (µFEA). The advantages of imaging with HR-pQCT compared to conventional imaging techniques can enable the possibility to analyse bone healing and the progression of bone healing in time in patients treated with BonAlive.

Study objective

This study focuses on the evaluation of Bonalive in bone defect healing and osteomyelitis treatment and it aims to investigate the bone healing capacity of BonAlive bioactive glass in patients who underwent debridement surgery in osteomyelitis treatment. This bone healing will be assessed using (HRpQCT) at 2, 6,12, 26, 52 and 104 weeks postoperative. In order to investigate the bone healing capacity specific parameters will be analysed. Furthermore in order to assess the longitudinal evolution of bone density trabecular bone and cortical bone density will be compared over time based on HRpQCT images which will also be used to assess the bone architecture over time the bone volume density, the number of trabeculae and trabecular thickness will be analyzed. Osteomyelitis treatment ie eradication of infection will be measured by comparing the infection parameters(CRP and ESR) in blood samples pre-operatively and during follow.Thereby we will also evaluate outcomes as pain, patient satisfaction and quality of life using te evaluation of different questionnaires during follow up.

Study design

Prospective longitudinal outcome study.

In this prospective longitudinal observational outcome study the clinical application of BonAlive bioactive glass for attaining bone healing, in patients with osteomyelitic bone defects due to debridement surgery, will be assessed. We will include patients who underwent debridement surgery combined with BonAlive implantation in a previous experimental study in order to assess the longitudinal results of the bone healing capacities until a maximum of 24-months after surgery. Assessment of bone healing capacities will be studied using HR-pQCT imaging techniques, where high-resolution imaging enables us to evaluate the micro-architecture and strength of bone several times during follow-up. All patients will undergo six HR-pQCT scans at 2, 12, 26, 52 and 104 weeks after surgery. Eradication of infection will be assessed by taking bloodsamples for analysis of the infectious parameters CRP and ESR previous to surgery and at 2, 6, 52 and 104 weeks after surgery leucocytes count direct postoperative and after 6-52-104 weeks. Clinical outcomes about pain, function and satisfaction will be assessed by using VAS-scores, SF-36 questionnaires and EQ-5D questionnaires at 6, 52 and 104 weeks post-operative and will be compared to pre-operative questionnaires. During this study we aim to include at least 20 patients.

Intervention

not applicable

Study burden and risks

After surgery the patient must return six times for outpatient monitoring. This is 2x more than the average patient in the regular treatment control would visit the hospital. During these checks, the patient receives several studies, such as blood tests, x-rays and HRpQCT scans. Also, he / she will occasionally have to fill out questionnaires. The burden and duration of these studies varies for the single patient. The duration of these various studies is: HRpQCT Scart 30 minutes, questionnaires (prior to be sent to the patient) to fill 15 minutes, consult orthopedic surgeon 15 minutes, X-rays 15 minutes, blood samples 15 minutes. The visits to the hospital take a minimum of 45 minutes and a maximum of 75 minutes.Thereby it will take some time to travel to the hospital. Participation in this study provides an (relatively small) additional burden for the patient, but simultaneously the patient is monitored better.

All patients participating in this study are at risk for risks associated with the operation. These patients will undergo a surgical debridement and bone reconstruction with BonAlive bioactive glass in combination with adjuvant treatment with antibiotics to treat osteomyelitis. The potential risks for these osteomyelitis treatment include: bleeding (with possibly a blood transfusion as a result), post-operative wound problems, post-operative pain,

fractures of the bone lesions, neurological damage, persistent wound leak and persistent or recurrent infection. However, the potential benefits from osteomyelitis surgery are bigger (in general) than the risks of surgery and monitoring.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P.Debeyelaan 25
Maastricht 6229 HX
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P.Debeyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients eligible for inclusion in this study are scheduled to undergo osteomyelitis debridement surgery combined with implantation of BonAlive bioactive glass at MUMC+.
;Inclusion criteria:
Subjects meeting all of the following criteria will be included in the study.;1. Patients with chronic (>12 weeks) osteomyelitis located in the distal tibia, distal fibula, ankle or foot. Or located in de distal radius, distal ulna, wrist or hand.

2. Patients who are scheduled to undergo osteomyelitis debridement surgery combined with implantation of BonAlive bioactive glass at MUMC+.
3. Patients that have normal contralateral bone, which will be used as an internal control.
4. Patients who accepted and signed the ethics committee approved informed consent before the first HR-pQCT scan.
5. Male and non-pregnant female patients between 18-70 years of age.
6. Patients who are physically and mentally able and willing to comply with the regulations of this study.
7. Patient can read and understand the Dutch language.

Exclusion criteria

Subjects meeting any of the following criteria will be excluded from the study.;1. Patients who are unwilling to cooperate with the study protocol and follow-up schedule.
2. Patients with chronic osteomyelitis associated with fracture in need of osteosynthesis surgery
3. Patients who, as judged by the surgeon, are mentally incompetent or are likely to be non-compliant with the prescribed post-operative routine and follow-up evaluation schedule.
4. Obese patients where obesity is severe enough to affect subject*s ability to perform activities of daily living (body mass index, kg/m2 > 40)
5. Patients with malignancy - active malignancy within last 1 year
6. Patients known with a diagnosed systemic disease that would affect the subject*s welfare or overall outcome of the study (severe osteoporosis requiring medication, Paget*s disease, renal osteodystrophy, hypercalcaemia) or is immunologically suppressed, or receiving steroids in excess of physiologic dose.
7. Patients with systemic or metabolic disorders leading to progressive bone deterioration.
8. Has received drugs that may interfere with bone metabolism within two weeks prior to the planned surgery date (e.g., steroids or methotrexate) excluding routine perioperative, non-steroidal anti-inflammatory drugs.
9. Patients with a known sensitivity to, specific antibiotics or radiation.
10. Patients under age of 18 and above age of 70
11. Females who wish to become pregnant before, during or after (up to two years) the course of their treatment.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-01-2019
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	05-07-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL56189.068.16