Enhancing distraction osteogenesis with CFR-PEEK bone pins and a 3D printed transfer device to permit artefact-free three-dimensional magnetic resonance imaging

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Abstract:

Objectives:

To: (1) design an artefact-free 3D-printed MR-safe temporary transfer device, (2) engineer bone-pins from Carbon Fibre Reinforced (CFR-PEEK), (3) evaluate the imaging artefacts of CFR-PEEK, and (4) confirm the osteointegration potential of CFR-PEEK, thus enhancing 3D-planning of bony advancements in hemifacial microsomia using sequential MRI.

Study Design:

Engineered CRF-PEEK bone pins and a 3D printed ex-fix device were implanted into a sheep head and imaged with MRI and CT. The osseointegration and bony compatibility potential of CFR-PEEK was assessed with Scanning Electron Microscopy (SEM) images of MC3T3 pre-osteoblast cells on the surface of the material.

Results:

The CFR-PEEK pins resulted in a signal void equivalent to the dimension of the pin, with no adjacent areas of MR-signal loss or CT artefact. MCT3 cells adhered and proliferated on the surface of the discs by forming a monolayer of cells, confirming compatibility and osseointegration potential.

Conclusion:

A 3D printed transfer device could be utilised temporarily during MRI to permit artefact-free 3D planning. CFR-PEEK pins eliminate imaging artefact permitting sequential MRI examination. In combination, this has the potential to enhance distraction osteogenesis, by permitting accurate three-dimensional planning without ionising radiation.

Key Words: Distraction Osteogenesis; Three-dimensional printing; Magnetic Resonance Imaging; Hemifacial Microsomia; Mandible; Osseointegration;

Introduction:

Craniofacial microsomia is a developmental anomaly of the first and/or second pharyngeal arch, and is considered to be the second most common congenital facial condition following cleft lip and palate [1]. Mandibular involvement is a continuum from hemi-hypoplasia through to abnormal configuration, with absence of the condyle and ramus. Unilateral asymmetry poses particular surgical challenges. Distraction osteogenesis is typically employed to lengthen the mandible and provide gradual increase in size of the soft tissue envelope. Planning the three-dimensional (3D) mandibular advancement is often reliant upon two-dimensional projections of anatomy through the use of radiographs in an attempt to minimise radiation exposure in young patients. The stainless-steel or titanium distraction device and pins result in significant metallic streak artefact limiting the use of 3D imaging with cone-beam or conventional computed tomography (CT) for sequential mapping of bony advancement, and stainless-steel devices are largely contraindicated in magnetic resonance imaging (MRI). Even if streak artefacts were eliminated on CT, the potential adverse effects of ionising radiation in these young patients raise serious ethical concerns in terms of repeated exposure to monitor and predict subsequent distraction advancements. A non-ferrous, artefact-free distraction device would permit sequential non-ionising imaging with MRI, thus opening up the possibility of accurate 3D planning of bone and soft tissue advancements. The incorporation of MRI “Black Bone” and ultra-short echo time techniques (such as gradient echo (GRE) techniques including 3D volumetric interpolated breath-hold (VIBE), as well as zero-echo time (ZTE) and pointwise encoding time reduction with radial acquisition (PETRA) sequences) provide not only the potential for 3D reconstructed imaging of the bone of the craniofacial skeleton but also the option for multi-planar reconstruction of the acquired volume [2-8].

Polyether ether ketone (PEEK) is increasingly being utilised as an alternative to more traditional screws and implants made from titanium or stainless steel [9]. Reported clinical outcomes are comparable to traditional devices, with the added benefit of minimising imaging artefacts. The addition of carbon fibre to form reinforced-PEEK (i.e. CFR-PEEK) improves the mechanical properties of the PEEK. With potential for osseointegration, CFR-PEEK distraction pins may offer similar capabilities to currently utilised titanium or stainless-steel distraction pins [10], but have not been explored for cranio-maxillofacial applications.

We hypothesised that CFR-PEEK pins would permit artefact-free (and ionising radiation-free) MRI examination, thus enhancing 3D planning of sequential bone advancements. Whilst recognising that some surgeons prefer intra-oral devices for mandibular distraction, the ease with which external fixator distractor devices can be removed from the distraction pins lends itself to the option for replacement with a temporary holding device for use during imaging acquisition, and provides a good starting point for initial investigation.

The objectives of this study were therefore four-fold: (1) to design a distraction device that could be used as a temporary device during MRI examination which was artefact free, (2) to engineer bone pins from CFR-PEEK, (3) evaluate the imaging effects of CFR-PEEK in comparison with titanium on multi-planar and 3D reconstructed imaging, and (4) confirm the osteointegration potential of CFR-PEEK.

Materials and Methods:

Design

Utilising standard mandibular distractor pins as the starting point, we engineered distractor bone pins from CFR-PEEK with a diameter of 3mm. Comparable pins of 3mm were engineered from titanium. A temporary external-fixator (ex-fix) transfer device was designed (SolidWorks, Dassault Systems, France) so as to permit easy transfer onto the distraction pins whilst permitting access for removal of the metal distraction device. The temporary device was 3D printed in translucent acrylic-based resin using stereolithography (SLA - Formlabs, Masshachusetts, USA), and thus MR-safe.

Radiological Imaging

To ascertain the associated imaging artefacts of the device and pins, four CFR-PEEK pins were implanted into the mandible of a dead animal model (sheep head) and the transfer device attached. MRI was acquired on both 1.5T and 3T magnets (GE MR450w and GE PETMR, GE Medical Systems Ltd, Buckinghamshire, UK) and 1.5T magnet (Siemens Prisma Fit, Siemens Healthcare Limited, Erlangen, Germany)). The imaging protocol included a “Black Bone” GRE sequence [2,3] and ZTE on both 1.5 and 3T GE systems, and PETRA and VIBE on a 1.5T Siemens system. In addition, T2 FLAIR and FSPGR imaging was acquired on a 3T magnet following the insertion of a 10mm CFR-PEEK rod into the mouth of the sheep alongside the distraction device. Comparable CT imaging was acquired with bone and soft tissue algorithms. The imaging protocol was repeated on a second animal model with four titanium pins and the temporary distractor device, and on a third animal model with one CFR-PEEK and one titanium distraction pin on the same side of the mandible. A fourth animal was imaged without intervention to provide a control. Conventional stainless-steel distraction devices and pins could not be evaluated in view of their non-MRI compatibility due to instability in the animal model.

MRI and CT artefacts were assessed on multiplanar imaging. Using 3D multi-planar reformats, the mandible was visualised at the point where the pins were crossing parallel to the bone, and the image magnified. The maximum diameter of the signal void for each of the four pins was measured using Osirix (Osirix MD, Version 10.0.5, Pixmeo SARL, Switzerland) and a mean result obtained. Three-dimensional reconstructed images of the skull and facial skeleton were produced using manual segmentation on Fovia (Fovia *High Definition Volume Rendering*©, Fovia Inc, Palo Alto, CA) using previously described segmentation techniques [1,2].

Cell Seeding

CFR-PEEK discs with an outer diameter of 10 mm and thickness of 0.5 mm were prepared. The specimens were sterilised using a standard autoclaving protocol. Samples were surface treated using oxygen plasma for 5 min to increase hydrophilicity of samples and thus encourage cellular interactions [11]. MC3T3 cell line (osteoblast precursor cell line derived from mouse calvaria) was cultured in polystyrene flasks in Dulbecco's modified Eagle's medium (Gibco®, Life Technologies Ltd., Paisley, UK) supplemented with 10% foetal bovine serum (FBS), 50 IU/ml of penicillin and 50 µg/ml of streptomycin at 37 °C. Confluent cells were then passaged by using trypsin-EDTA (Invitrogen, Paisley, UK) over the CFR-PEEK discs.

Scanning Electron Microscopy (SEM) Images

Specimens were fixed in 3% glutaraldehyde and 0.1M cacodylate buffer and stored at 4˚C overnight. Serial ethyl alcohol dehydration was carried out the next day for 10 min at each concentration and the discs were subsequently dried in hexamethyldisilazane and left in the hood for 1 hour. Specimens were then coated with 95% gold and 5% palladium (Polaron E5000 Sputter Coater, Quoram Technologies, Laughton, UK) and SEM (Philips XL30 Field Emission SEM, Amsterdam, Netherlands) was used to visualise the surface of the specimen discs.

Results:

The temporary ex-fix transfer device with CFR-PEEK pins in-situ in the sheep head, the CFR-PEEK and titanium pins are shown in **Figure 1**. As demonstrated in **Figure 2a-d**, the CFR-PEEK pins, 10mm rod and transfer device could be visualised on CT, but did not result in any streak-artefact.

The transfer device was not visualised on any of the MRI sequences and the CFR-PEEK pins and rod were visualised as an area of signal void (**Figure 3**). The necessary drilling into the mandible to insert the distractor pins resulted in the introduction of a small volume of air, which is also seen as an area of signal void on all MRI sequences; this artefact was reduced on ZTE/PETRA sequences. The increased signal void due to the presence of air is further shown in **Figure 4**, where the 10mm CFR-PEEK rod is shown in contact with air within the oral cavity. Measurement of the CFR-PEEK rod on FLAIR and FSPGR sequences and CT imaging at sites distant from air were comparable, and correlated with the known 10mm diameter.

The titanium pins resulted in increased artefact on all MRI sequences, with an increased mean measurement for the intraosseous signal void resulting from the distraction pins equating to, on average, double the diameter of the pin (**Table 1, Figure 3**). CT maximum interpolation images (MIP) (**Figure 2e-g**) demonstrate the pins and transfer device across the three sheep heads to highlight the volume of metalwork in the 2nd head. In this case, where there were four titanium pins this resulted in notable streak artefact on CT (**Figure 5**).

The “Black Bone” sequences in view of their volume acquisitions permitted multi-planar reformats of the bone at any angle, thus providing optimal visualisation of the mandible and distraction devices, comparable to CT. In addition, the MRI data was used to successfully produce 3D reconstructed images of the mandible (**Figure 6**) to further highlight the benefit of the artefact-free devices.

The non-toxicity of the CFR-PEEK and its osseointegration potential were confirmed with SEM images (**Figure 7**). The morphology and proliferation of MC3T3 cells on the surface of the discs were successfully observed. This showed formation of a monolayer of cells with apparent cell morphology, where the process of cell division could also be detected. The overall cell alignment exhibited an elongated and uniform network covering the surface of the material.

Discussion:

Titanium metal alloys are frequently used in surgery because of their relatively low magnetic susceptibility artefact when compared with stainless steel [9-10,12-14]. Titanium offers a similar material strength to stainless steel at reduced weight, which combined with its biocompatibility and osseointegration makes it ideally suited to implanted medical devices. However, its significantly increased elastic modulus compared to bone may result in bone resorption and implant fracture [15]. PEEK was originally developed by the aerospace industry with potential for high-load, high-temperature applications. By the late 1990’s PEEK was increasingly utilised as an alternative to conventional metallic implants in view of its biocompatibility and improved compatibility with diagnostic imaging. In addition, it has been shown to cause fewer hypersensitive and allergic reactions than titanium [15]. Carbon-fibre-reinforced polyether ether ketone (CFR-PEEK) has a modulus very similar to bone and an ability to withstand prolonged fatigue strain, and may be able to avoid potential issues such as stress shielding and bone resorption [10]. To our knowledge, unlike PEEK, CFR-PEEK has not previously been described in the literature for cranio-maxillofacial applications.

We have demonstrated the potential benefit of a temporary distraction device and CFR-PEEK distraction pins which result in minimal signal void on MRI sequences, and absence of streak artefact on CT. The MRI sequences explored are amenable to multiplanar and 3D reconstruction and therefore provide a feasible alternative to CT imaging. 3D reconstructed images of the mandible were created using manual segmentation techniques for this study. We have previously reported our automated segmentation algorithms, which were not transferrable to the sheep heads, but would be applicable in clinical practice providing excellent potential for 3D visualisation of bony advancements [16, 17].

GRE sequences resulted in increased artefact from adjacent air compared to the ZTE sequences. However, this is unlikely to be problematic in routine imaging since the post-operative air would be either resorbed or replaced with tissue fluids e.g. blood. No artefact was seen on CT imaging with the CFR-PEEK pins. In comparison, despite their small diameter the titanium pins resulted in noticeable streak artefact on CT, and were associated with an increased area of signal void on all MRI sequences.

Investigating cellular morphology is a practical approach in evaluation of osteogenic potential of biomaterials. Cell interaction with the material surface, in the complex process of cell attachment, can also determine osseointegration. In this study cell proliferation demonstrated on electron microscopy proposes the potential for osseointegration of the CFR-PEEK discs. This can be beneficial in distraction pins to maintain stability, permit accurate bony advancements and prevent migration of the pins. However, in order to confirm the findings, assessment of cell metabolic activity and DNA content can provide a more accurate indication of how the cells respond to the material surface.

With the potential for osseointegration, CFR-PEEK pins provide a viable alternative to titanium or stainless steel bone pins, which when used in combination with a 3D printed temporary transfer device, yields artefact-free imaging to enhance 3D planning of sequential bone advancements. The use of the temporary 3D printed distraction device is of course only possible when utilising a traditional external fixator device, which permits easy replacement of one holding device for another prior to and following imaging. It is recognised however that there has been a general shift in practice toward using internal distractor devices which are held in place with integral mini-plates. Replacing these more complex designs with CFR-PEEK would require the entire device to be manufactured from this newer material. Further investigation is required to determine the feasibility of engineering such complex designs.

In conclusion, we have demonstrated the potential benefit of utilising artefact free distraction pins and a temporary distraction device, which would permit enhanced sequential planning of mandibular advancements using 3D MRI techniques.

Figure Legends:

Figure 1: (A) CRF-PEEK distraction pin and four pins held within the temporary ex-fix transfer device which was 3D printed in PolyJet resin; (B) the CRF-PEEK pins and temporary ex-fix transfer device in situ within the mandible of a sheep; (C) corresponding titanium pin and four pins held within the transfer device; (D) 10mm CRF-PEEK rod; and (E) CRF-PEEK distraction pin (top) and comparable titanium pin (bottom).

Figure 2: (A) Oblique axial bone algorithm CT imaging showing the absence of artefact from the CRF-PEEK pin and temporary transfer device, (B) oblique coronal soft tissue algorithm CT again demonstrating the CRF-PEEK pin and transfer device, with a 10mm CRF-PEEK rod within the left maxillary buccal sulcus, (C) 3D volume rendered CT bone image showing the non-visualisation of the CRF-PEEK pins and transfer device compared to the 10mm CRF-PEEK rod, (D) 3D volume rendered CT soft tissues to demonstrate the CRF-PEEK pins, rod, and transfer device in situ. CT maximum intensity projection (MIP) imaging of the sheep head with (E) 4 CRF-PEEK distraction pins with transfer device, plus 10mm CRF-PEEK rod, (F) four titanium distractor pins and (G) one CRF-PEEK (anterior) and one titanium (posterior) distraction pin.

Figure 3: Oblique axial MRI images of the CFR-PEEK distraction pin from (A) 1.5T ZTE, (B) 1.5T GRE BB, (C) 3T ZTE, (D) 3T GRE BB, (E) 1.5T PETRA and (F) 1.5T VIBE. Oblique axial imaging of the mandible demonstrating the artefact associated with the 4 titanium pins on (G) 1.5T ZTE, (H) 1.5T GRE BB, (I) 3T ZTE, (J) 3T GRE BB, (K) 1.5T PETRA and (L) 1.5T VIBE.

Figure 4: 10mm CRF-PEEK rod within the left maxillary buccal sulcus on (A) CT bone algorithm, (B) 3T FLAIR and (C) 3T FSPGR imaging, demonstrating the absence of artefact, and inability to distinguish air from the CRF-PEEK on FSPGR imaging.

Figure 5: CT imaging of the sheep head with four titanium distractor pins and temporary transfer device in-situ. This demonstrates metallic streak artefact (arrows) seen on both bone algorithm (A&B) and soft tissue algorithms (C&D).

Figure 6: 3D volume rendered BB image of the craniofacial skeleton of the first head with non-visualisation of the CFR-PEEK pins, rod, and temporary transfer device.

Figure 7: SEM images showing the attachment and proliferation of MC3T3 cells on the surface of CFR-PEEK discs at two different magnifications

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Figure 1

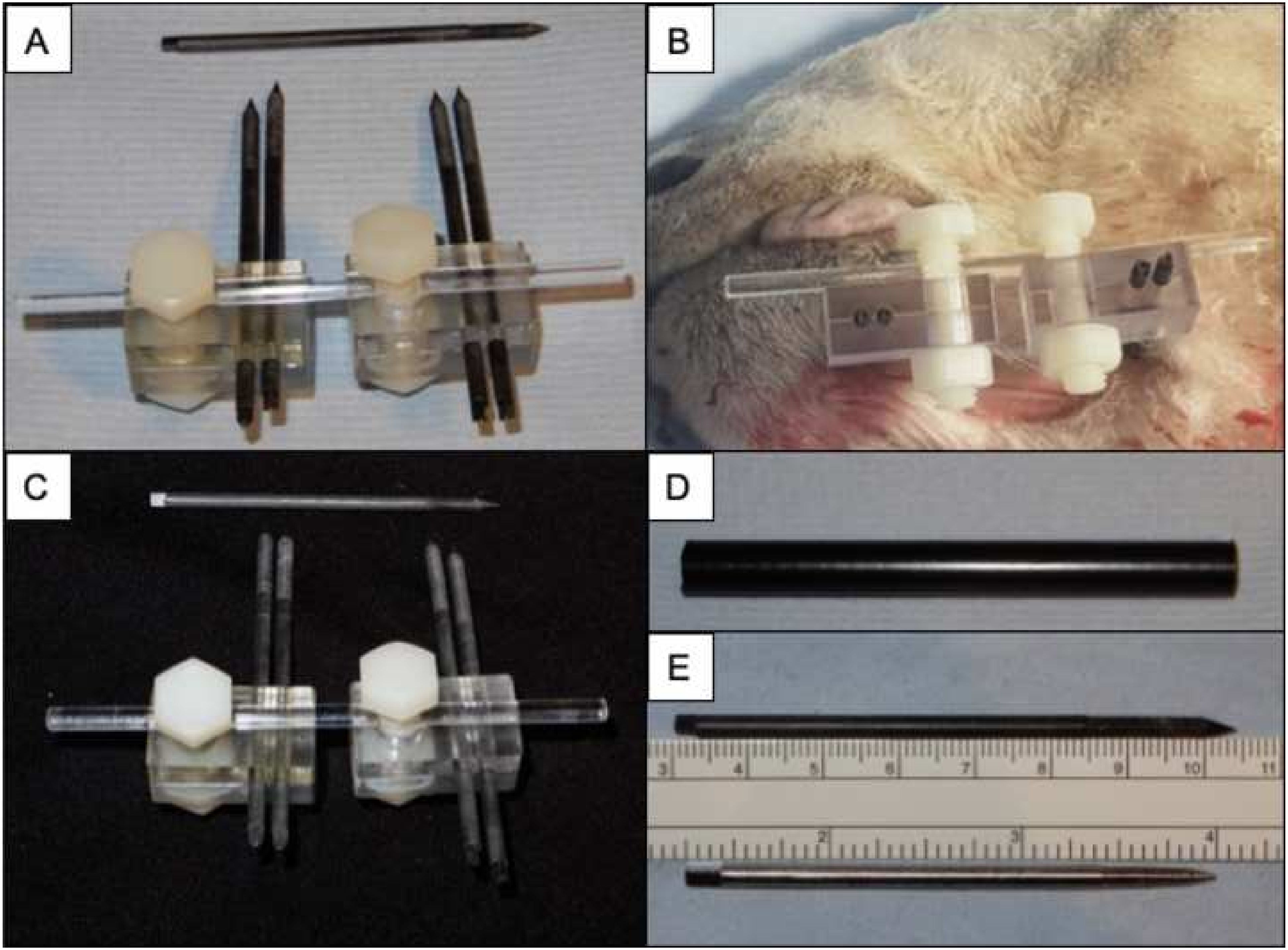

Figure 2

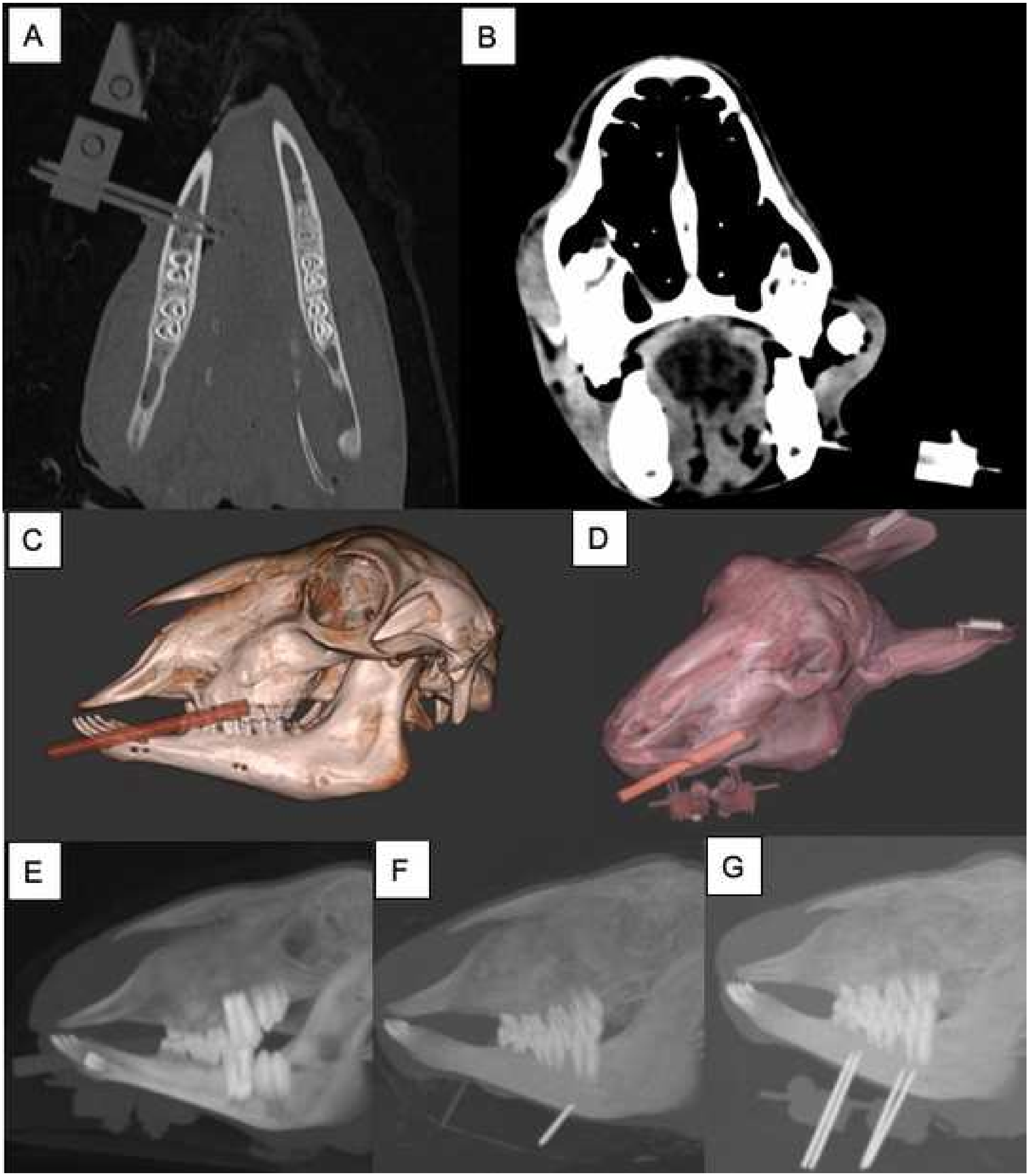

Figure 3

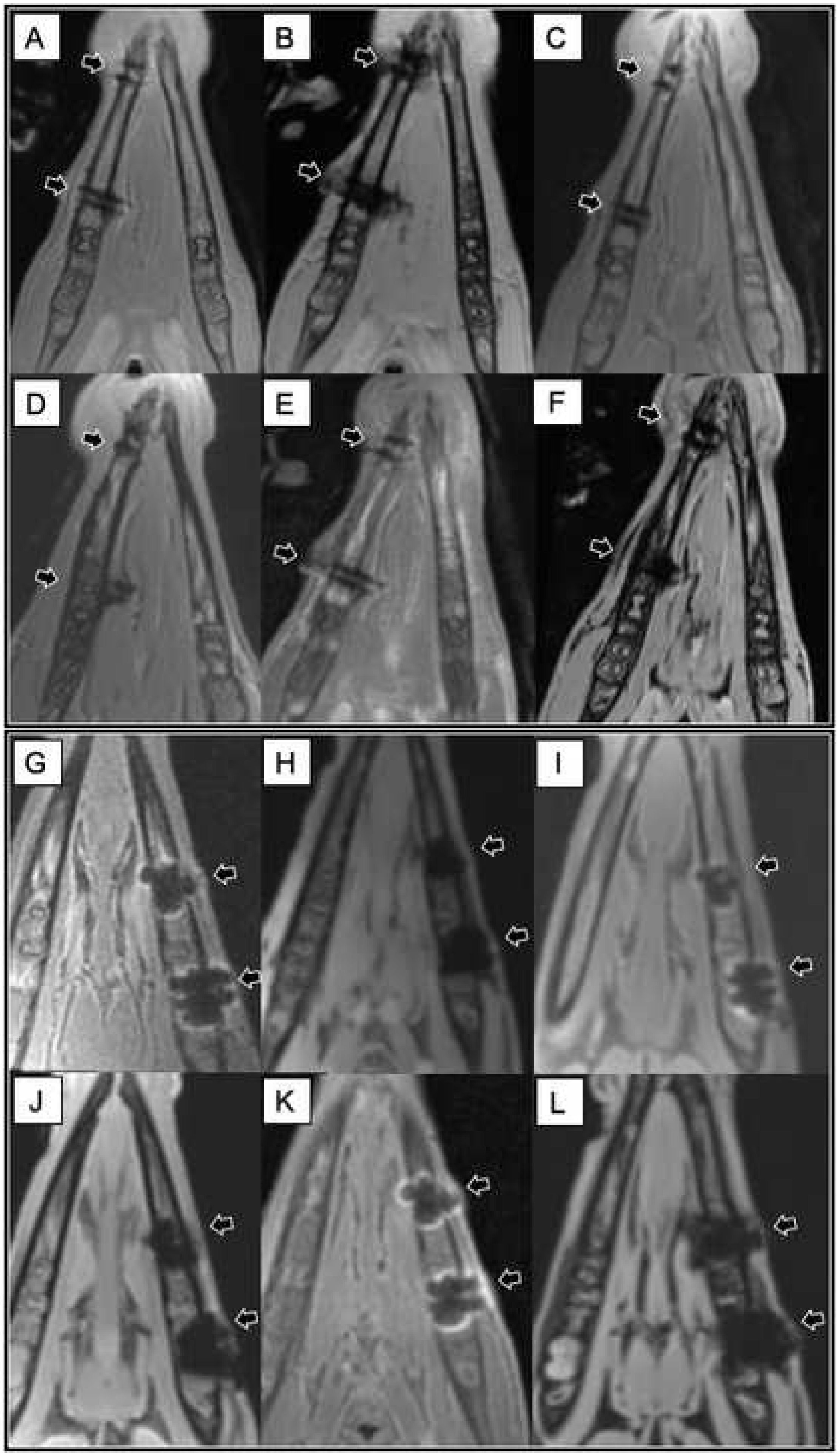

Figure 4

Figure 5 Click here to access/download;Figure (1 Figure per File. DO NOT embed image in TEXT);Figure 5.jpg

Figure 6

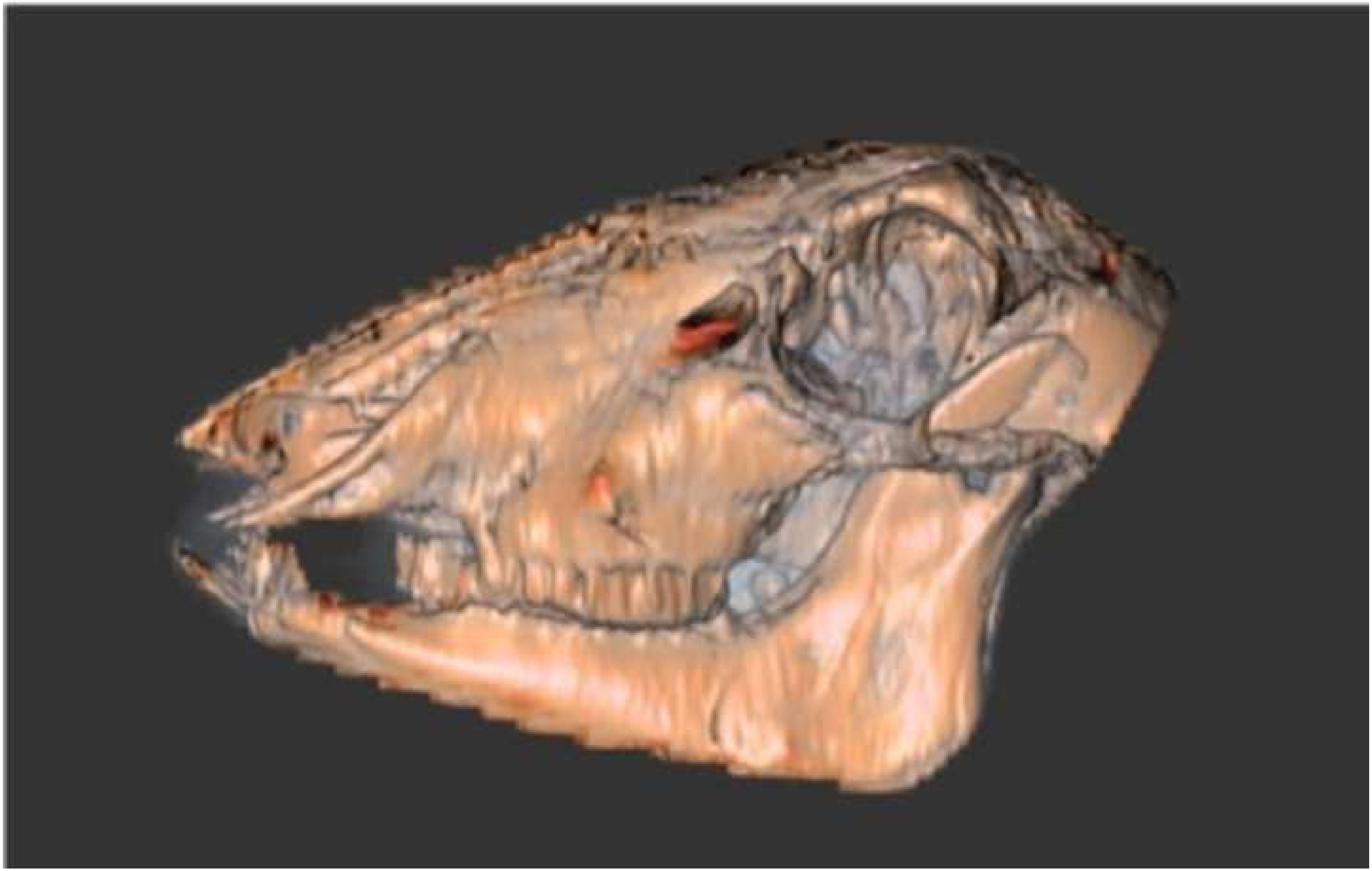

Figure 7

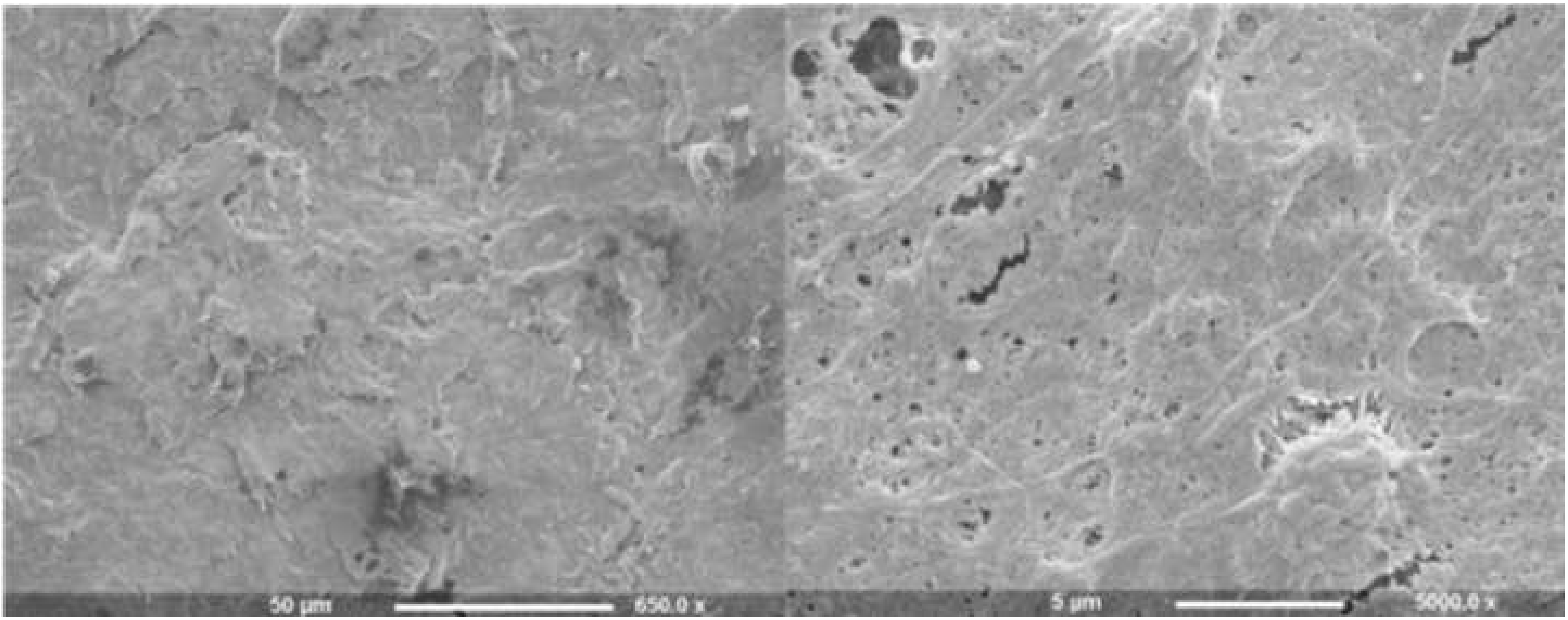

Table 1: Mean measurement of the intraosseous signal void for the four 3mm distractor pins measured on each of the MRI sequences, in mm.

	Titanium	CRF-PEEK
1.5T BB	5.19	3.26
1.5T ZTE	6.04	2.35
1.5T VIBE	5.52	2.87
1.5T PETRA	4.35	2.37
3T BB	7.38	2.84
3T ZTE	5.47	2.17