A Novel Near Infra-red Fluorescent Probes to Repair Metal Artifact After Implantation

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ABSTRACT

Accurate, noninvasive techniques for monitoring bone-implant integration are demanded in clinic. Standard X-ray and CT provide a snapshot of the skeletal structure. However, metal artifact is an unsolved problem to visualize the CT image detail of the bone tissue around metal implants. Therefore, evaluation of new bone formation or implant failing after an implantation surgery became difficult in clinic. The need led scientists to develop a nano-imaging probe to precisely reveal osseointegration with implants. Conjugation of near infra-red fluorochrome (NIRF) CyTE-777 with α5β1 integrin specific binding peptide GGCRRETAWAC, a α5β1 targeting NIRF probe was synthesized for the molecular imaging of osteoblastic activity and bone repair in vitro and in vivo. NIRF signals were significantly observed in activiated MG63 osteoblasts, and surgically implanted-mice. Three to four weeks after the implantation in mice, NIRF image can functionally recover the artifact data at implant sites of the CT image. The novel nano imaging technique provides a useful tool for monitoring the extent of osteogenesis in the surrounding bone tissue at the implantation site. Combined with CT, this approach might repair the image loss by metal artifact, and further predict the fate of the implantation in clinic.

Keywords: implant, metal artifact, nano imaging, NIRF probe

INTRODUCTION

Metal artifact presents as an unavoidable problem, which affects the quality of the image during CT scanning. When metal implants are present in the field of measurement, it causes fake signals or metal shadows which significantly interferes the obtained data. The current solution to reduce the metal artifact is to replace the altered projection image by interpolation which cannot completely recover the lost information[1]. In the orthopaedic and dental surgery, osseointegration of the implant and the surrounding tissue is a critical factor to success implantation[2-5]. However, it is hard to evaluate the osseointegration of metal implants simply by CT image, while a 10 μm image gap around the implants due to data lost results from metal shadow. The purpose of this work is to develop a maxilla implant animal model to mimic the metal artifacts in human subjects[6]. Subsequently, pamidronate-NIFR probe was developed to reveal the bone regeneration site around the implants. As combined with the CT image data, a new approach could be developed to solve the image lost problem result from metal shadow.

SD rats were used to investigate the CT artifact of titanium implants. Titanium screws were placed into the maxilla bones as recipient sites in rats and the animals were euthanized for micro CT analysis. The established animal model was applied to examine the metal artifact caused by the titanium screws, and to combine novel NIRF probes to evaluate the extent of osteogenesis at the implant site.

MATERIALS and METHODS

SD rats were implanted with titanium screws in the hard plates of the maxilla bone. Animals were examined by X-ray, CT to obtain morphological data of the implanted site 28 days after the surgery. The animals were then injected with a pamidronate-conjugated nanogold NIRF probe which can specifically binds to the new bone formation site, by which the fluorescence signals were acquired on an NIFR imaging system using an excitation wavelength of 610-650 nm and an emission wavelength of 680-720 nm.

ANIMALS

Briefly, Six 6-month-old SD rats will be housed in a laboratory at 22.2°C under a 12-h light and 12-h dark cycle and fed ad libidum. All animals are treated according to the guidelines and regulations for the use and care of animals. Titanium screws of 1.2 mm

(diameter) × 2.4 mm (length) was placed into the hard plate of the maxilla of the animals. Animals were followed by X-ray, micro-computed tomography and IVIS-200 at 28 days after the surgery.

CT ANALYSIS

For micro-CT scan of implantation, SD rats were maintained under general anesthesia during the scanning procedure. Each animal is placed in a sample holder in the cranial-caudal direction and scanned using a high-resolution micro-CT system (Triumph X-O CT System) at a spatial resolution of 80 μm (voxel dimension) and 1024 × 1024 pixel matrices. The peri-implant bone image is acquired using AMIDE software.

IN VIVO NIRF IMAGE

Twenty-eight days after the surgery, each mouse was injected with 20 nM of pamidronate-NIRF probe systemically. Twenty-four hours later, the animals were anesthetized with isofluorane and taken NIRF imaging using a IVIS-200 imaging system with an excitation and an emission bandpass filter of 610-650 nm and 680-720nm, respectively.

STATISTICAL ANALYSIS

To quantify the NIRF signal intensities, a circular region-of-interest (ROI) was manually defined surrounding the implant, and the average signal within this ROI was obtained. Data are presented mean$\pm$ SD. Statistical analysis of different groups was conducted using one-way ANOVA and Duncan test. A p-value $\leq$ 0.05 was considered to be significant.

RESULTS

Fluorescent signal was observed at the implantation site of the rats. NIFR fluorescent imaging of all animals showed approximately a 2.3-fold difference in signal intensity between new bone formation site and the normal tissue around the metal implants. The signal intensity can be used to repair the metal artifact in the CT image caused by the lost data.

CONCLUSION

The pamidronate-NIRF probing imaging showed a significant difference between the new bone formation site and normal tissue around the metal implant. The described pamidronate-NIRF probe offers a novel method for repair of the metal artifact in CT image.

ILLUSTRATION

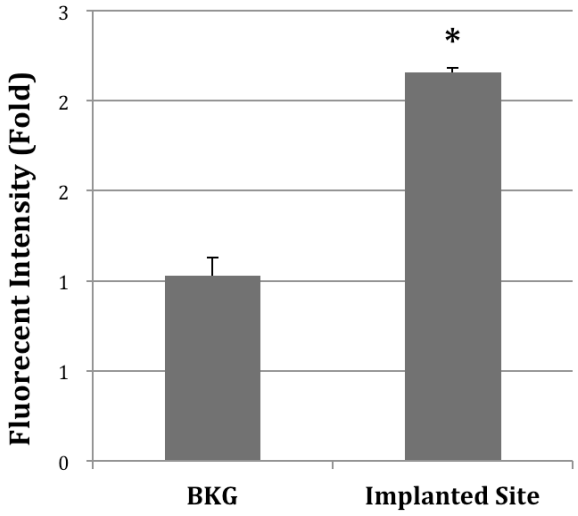

Figure 1: The fluorescent intensity of the implanted site versus background intensity in the maxilla of the titanium screw-implanted rats. The data indicated that the implanted site exhibits a significant 2.3 fold fluorescent intensity then the control (non-implanted background) site.

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