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Zirconia vs Titanium Dental Implants Demonstrate Superior Early Healing in Mice Assessed with PEGASOS Tissue Clearing and Two-Photon Microscopy

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Titanium dental implants have become a routine dental restoration over the past 2 decades, but the problem of titanium-induced peri-implantitis [1, 2] has led to a search for a non-metallic implant material such as zirconia. In this study we evaluated early healing of zirconia dental implants in mice. We crossed Cdh5-Cre^{ERT2} with Ai14 reporter mice to produce a lineage with an inducible label for angiogenesis. At 6-8 weeks of age, we extracted the maxillary first molars and placed either a titanium or a zirconia implant, Figure 1. After allowing 2 weeks for healing, mice were sacrificed and imaged with μCT radiography, cleared and processed using the PEGASOS protocol [3] prior to imaging with 2-photon microscopy. Both the zirconia and titanium dental implants healed well after placement in the mouse maxilla. We measured tdTomato fluorophore in the Cdh5 mice to quantify neovascularization around the implants which has been previously correlated with osseointegration [4]. The area of bone in the peri-implant area was similarly quantified by second harmonic generation (SHG), Figure 2. The zirconia implants demonstrated greater amounts of neovascularization compared to the titanium implants. Greater amounts of bone were also present around the zirconia implants compared to the titanium implants. Zirconia dental implants appear to be well tolerated in the oral cavity, and at least at this early timepoint, appear to be clinically equivalent to the more common titanium implants. When evaluated on a microscopic level, the zirconia implants demonstrated more exuberant vascular healing as well as improved levels of bone support in the peri-implant region.

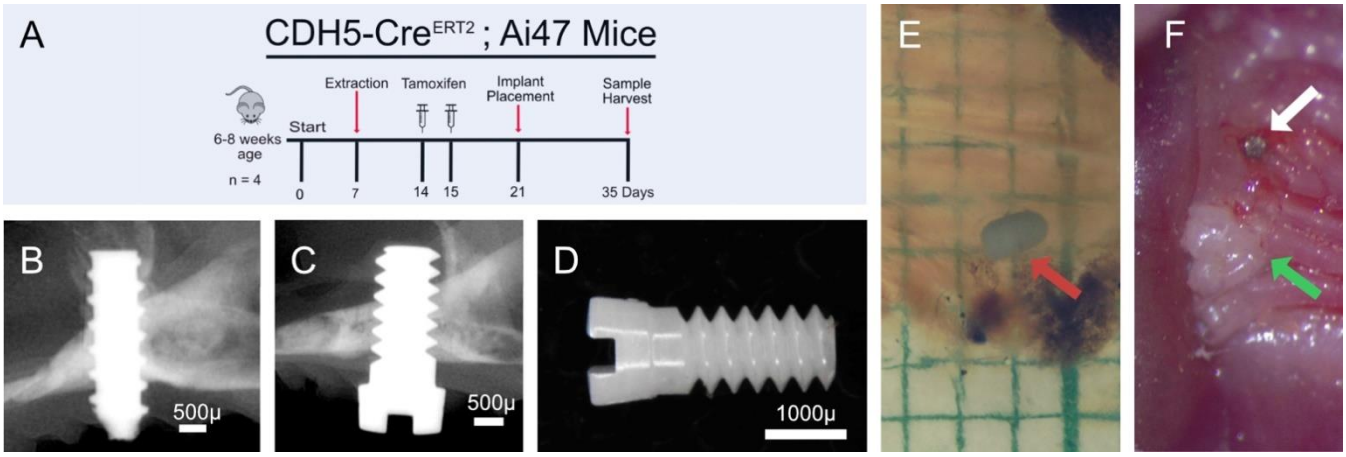

Figure 1. Experimental design and results. A) Timeline of the experiment. B) Radiograph demonstrating osseointegration of the titanium implant in the mouse maxilla. C) Radiograph showing osseointegration of the zirconia dental implant. D) Zirconia dental implant prior to placement E) Zirconia implant (red arrow) in mouse skull cleared with PEGASOS protocol in preparation for two-photon imaging, 1mm x

1mm grid. F) Photograph demonstrating location of implant placement in a healed first molar extraction site, titanium implant (white arrow) in relation to second molar (green arrow).

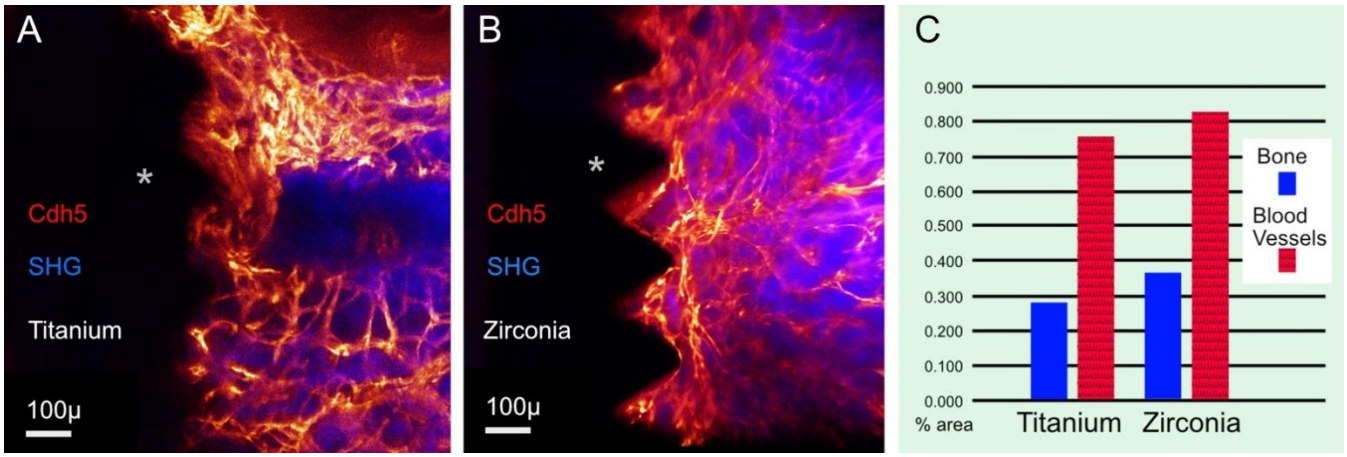

Figure 2. Assessment of dental implant healing at two weeks demonstrates increased bone (SHG) and neovascularization (Cdh5-tdTomato) around the zirconia implant vs titanium. A) Titanium dental implant imaged with 2-photon microscopy. (*) denotes implant. B) Zirconia implant. C) Quantitative assessment of healing demonstrating both an increase of bone and vasculature in the zirconia implants at 2-weeks vs titanium implants.

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