

and biology of transplanted stem cells in the living subject. Recent advances in molecular biology and imaging have allowed the successful non-invasive monitoring of transplanted stem cells in the living subject. The ideal imaging method should provide the information of (1) Real-time visualization of stem cell delivery; and (2) Determination of location(s) and Quantification of cells over time. The chosen labeling modality should not interact with the normal functions of the stem cell and provides a good contrast between background and the target signal under study, achieving a large signal-to-noise ratio. Reporter gene-bioluminescence imaging (BLI) is based on light emission and detection by specific cooled charge coupled device (CCD) cameras. Similar to other reporter gene strategies, the BLI signal is only emitted when cells are viable, and thus can be used for the longitudinal monitoring of stem cell survival and study of cell status. BLI has been successfully used for *in vivo* study of cell delivery and monitoring of stem cell viability, fate, interaction between stem cells and microenvironments in small living animals. We have investigated the distribution of systemically delivered luciferase labeled MSCs in fracture animal model and tumor bearing animals. The whereabouts of the labelled stem cells are monitored using the *in vivo* imaging system (IVIS 200, Exogen, USA), and accessed the efficiency of using stem cells therapy for promoting fracture repair (Fig. 1) and anti-cancer gene therapy.

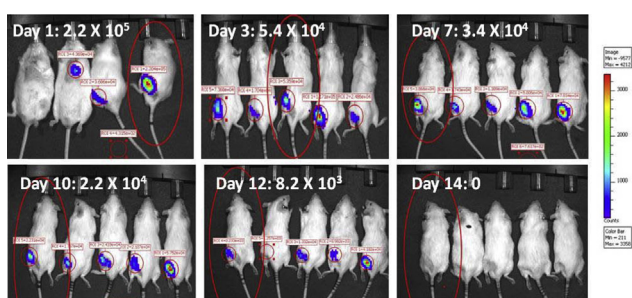


Fig. 1. Allogenic Luc-MSCs were injected into the fracture site in mice, and were monitored using *in vivo* imaging system. Allogenic MSCs became undetectable 14 days after injection. All animals did not show obvious adverse side effects.

Brief CV

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UPDATE ON OPTICAL IMAGING DEVELOPED FOR PRECLINICAL STUDIES OF BONE

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Optical imaging techniques are among the most powerful techniques in preclinical research, specifically for the imaging of rodents. It includes (i) methods suited for mesoscopic (spatial resolution of about 1 mm) whole body non-invasive imaging, specifically fluorescent and bioluminescent imaging, (ii) microscopic techniques, most notably multiphoton and confocal microscopy, and (iii) spectroscopic approaches such as Raman and Fourier Transform Infrared imaging and mass spectroscopy imaging.

A key reason for the attractiveness of optical imaging is the possibility to exploit the extremely powerful methods of genetic engineering. For example, transgenic mouse models can be generated that feature near infrared reporter signals associated with specific gene expression. By this mechanism of molecular imaging, morphologic imaging can be extended to *in vivo* functional imaging.

Optical imaging of bone is feasible but presents specific hurdles that to date have only partially been overcome. Light is strongly scattered and absorbed leading to strong attenuation and resulting limits in spatial resolution, decreasing rapidly with increasing depth. This also leads to bias in the quantitative evaluation of optical signals. On the positive side, due to the strong bone binding properties of bisphosphonates, bone labeling molecules have been developed. These bind to mineral on bone surface and permit *in vivo* insight into bone turnover. In this way, they work similar to serum markers of bone turnover, but they provide this information in a spatially resolved way, including 3-D depiction using fluorescent molecular tomography (FMT).

Ex vivo optical imaging provides powerful assessment tools specifically for the organic components of bone tissue. Second harmonic generation (SHG) is a contrast mechanism of multiphoton microscopy specific to collagen. Mineral to matrix ratios and subtype analysis of collagen is feasible with the aforementioned spectroscopic imaging approaches, promising to help elucidating bone fragility in secondary osteoporosis and other disorders, e.g. effects of diabetes on bone.

The goals for research in the coming years include the refinement of these methods, the linking of mesoscopic with microscopy techniques in order to obtain a comprehensive assessment of as many dimensions of bone quality as possible, the *in vivo* assessment of bone function down to the cellular level, in order to improve the assessment of bone metabolism and other skeletal disorders.

Brief CV

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Dr. Claus-C. Glüer is a Professor of Medical Physics at the Department of Radiology and Neuroradiology, University Hospital Schleswig-Holstein in Kiel, Christian-Albrechts-Universität zu Kiel, Germany. His research is aimed at the development of innovative parametric imaging techniques and their quantitative evaluation. Since 1987 when he started his postdoc in the *Osteoporosis Research Group* of Prof. Harry K. Genant at the University of California, San Francisco, Dr Glüer has focused his research on osteoporosis and other bone disorders. He has contributed specifically to the development of bone densitometry, quantitative ultrasound and high resolution computed tomography approaches. He has coordinated several multicentre studies including *OPUS*, a European project on epidemiology and optimised diagnostic assessment of osteoporosis.

Dr. Glüer also has a strong research interest in multimodal methods for molecular imaging with applications in oncology, inflammation, and skeletal research. He co-founded the *Molecular Imaging North Competence Center (MOIN CC)* at the *Christian-Albrechts-Universität zu Kiel*, a preclinical imaging lab. At *MOIN CC*, multi modal imaging studies combining micro computed tomography, high-field magnetic resonance imaging, high resolution ultrasound, fluorescence and bioluminescence imaging can be carried out to study morphological, functional, cellular, and molecular processes in health and disease and to assess therapeutic effects.

Dr. Glüer is the current president of the *German Society for Osteology (DGO)*, past president of the *German Academy of Bone & Joint Sciences (DAdorW)* and *President of the European Calcified Tissue Society*. He has published more than 175 original papers, 20 books and book chapters, and holds 3 patents

MUSCULOSKELETAL IMAGING TECHNOLOGIES IN R&D OF 3D BONE COMPOSITE SCAFFOLD BIOMATERIALS

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