

($P < 0.05$), and treatment-related toxicity was not observed in the pancreas and kidneys while slight glomerulopathy was detected.

The pharmacokinetic, imaging, and therapy studies suggest that the theranostic twins ($^{68}\text{Ga}/^{177}\text{Lu}$)-labeled bombesin derivatives have promising characteristics for application in nuclear medicine, namely, for the diagnosis and treatment of GRPR-overexpressing prostate tumors.

Keywords: Theranosis, Prostate cancer, Bombesin, Radionuclide

References:

- [1] Cescato, R., et al., Bombesin receptor antagonists may be preferable to agonists for tumor targeting. *J Nucl Med*, 2008. 49(2): p. 318-26.
- [2] Mueller, D., et al., Simplified NaCl based (^{68}Ga) concentration and labeling procedure for rapid synthesis of (^{68}Ga) radiopharmaceuticals in high radiochemical purity. *Bioconjug Chem*, 2012. 23(8): p. 1712-7.

138

The role of adipose stromal cells for reversal of radiation fibrosis

X. Zhao^{1,3}, P. Psarianos³, J.H. Lee, L³. Ailles, K. Yip⁴, F.F. Liu⁴

¹ Institute of Medical Sciences

² Department of Radiation Oncology

³ Department of Otolaryngology - Head and Neck Surgery

⁴ Princess Margaret Cancer Centre, University Health Network

Hypothesis: Radiation fibrosis (RF) effects up to 70% of patients who have undergone radiotherapy. It is characterized by irreversible scarring of normal tissue resulting in functional morbidity and increased risk of surgical complications. Adipose-derived stromal cells (ADSCs) are a subcategory of mesenchymal stromal cell. Much of the therapeutic benefit of ADSCs has been attributed to secretion of cytokines and growth factors involved in immunomodulation, cell survival, and metabolism. We hypothesize that ADSCs may be therapeutically effective for RF through reversal of metabolic aberrations.

Methods: A mouse model of RF was developed and ADSC isolation was confirmed by surface marker expression and by differentiation capacity down the mesenchymal lineage. GFP and luciferase labelled ADSCs were used to assess biodistribution and cell survival after transplantation. To determine the therapeutic effect of ADSC transplantation for RF, we assessed functional changes to tissue elasticity using a leg contracture measurement tool and to collagen deposition using trichrome blue staining. To determine the mechanism of ADSC-mediated fibrosis reversal, we assessed transcriptomic changes to RF tissue.

Results: A RF model was created by radiating the hind limb of C3H mice. This model showed a dose dependent leg contracture and histological findings of fibrosis. We confirmed the immunophenotype of isolated ADSC and their ability to differentiate into adipogenic, chondrogenic, and osteogenic lineages. ADSC transplantation showed a statistically significant trend towards improved leg contracture (2-way ANOVA, $p < 0.05$) and reduced collagen deposition. Biodistribution studies confirmed the presence of ADSCs in the subdermis of RF tissue with persistence for at least 18 days post-transplantation. Preliminary RNA-seq over-representation pathway analysis showed that lipid metabolism and PPAR γ signaling were among the top pathways down regulated in radiation fibrosis and was partially reversed with ADSC treatment. ADSCs directly reversed alterations to lipid metabolism in radiated fibroblasts through indirect co-culture.

Conclusions: ADSC transplantation may be an effective treatment for the reversal of radiation fibrosis through metabolic reprogramming. As cancer survivorship increases, the prevalence of radiation fibrosis will rise and necessitate increased focus on effective treatment strategies for this condition.

Keywords: Adipose Derived Stromal Cells, Radiation Fibrosis, Cancer Survivorship

139

Characterization and test beam results of a LaBr₃ Compton Telescope for treatment monitoring.

G. Llosá¹, J. Barrio¹, A. Etxebeste¹, C. Lacasta¹, J.F. Oliver¹, P.G. Ortega^{1,2}, C. Solaz¹, P. Solevi¹.

¹ Instituto de Física Corpuscular (CSIC/UVEG), Parque Científico. C/. Catedrático Beltrán, 2. E-46980 Paterna, Spain.

² CERN (European Organization for Nuclear Research), CH-1211 Geneva, Switzerland

Purpose: The detection of gamma rays for monitoring purposes can overcome some of the limitations of PET, since they are more abundant than positron emitters and are produced within nanoseconds after irradiations. However, their continuous emission spectrum up to high energies (more than 10 MeV) make their detection challenging [1]. Collimated systems and Compton cameras are being developed for this application.

The IRIS group of the Instituto de Física Corpuscular (IFIC-CSIC/UVEG, Valencia) has developed a three-layer Compton telescope based on LaBr₃ scintillator crystals for hadron therapy monitoring within the ENVISION project.

Materials and Methods: The telescope consists of three planes of LaBr₃ crystals, which provide high energy resolution and fast response, coupled to silicon photomultiplier arrays. A custom made data acquisition system has been developed to read out the detectors and operate them in time coincidence, employing the VATA64HDR16 ASIC[2]. The system aims at combining two- and three-layer events in order to profit from the high efficiency of the former and the high precision of the latter. The functionality of the device has been tested in the laboratory with radioactive sources, and also in beam tests. A dedicated image reconstruction ML-EM code has also been developed for both types of events.

Results: The system has been characterized in the laboratory acquiring data with radioactive sources of different energies. The detector response in terms of linearity, uniformity and spatial, energy and timing resolution has been obtained for the three layers, improving the results of the first tests. In addition, images of a point-like Na-22 source have been reconstructed with two and three-layer systems. The preliminary spatial resolution obtained is 7.3 mm FWHM with the two-layer system and 8.6 mm FWHM with the three-layer system.

The two-layer system has also been tested in a proton beam at KVI-CART, Groningen. Data were taken with a 150 MeV proton beam with an intensity of about 10^9 protons/s and a lateral beam spread of 5.3 mm impinging on a PMMA phantom. The PMMA target was placed in two different positions along the beam separated by 10 mm. The data analysis and image reconstruction of the data have shown a difference in the reconstructed profile consistent with the phantom position [3].

Conclusions: The laboratory tests carried out assess the correct functioning of the device. In-beam results show the capability of detecting range shifts. Current work is focused on performance improvement of the system and on simultaneous operation of two and three detector layers. Further tests in beam are planned at HZDR Dresden for December 2015.

Keywords: Compton Telescope, Hadron therapy, treatment monitoring.

References:

- [1] Roellinghoff, F. et al. Design of a Compton camera for 3d prompt-imaging during ion beam therapy. *Nuclear Instruments and Methods A* 648, S20-S23.
- [2] Trovato, M., Solevi, P., Torres-Espallardo, I., Gillam, J., Lacasta, C., Rafecas, M., et al. A three layer Compton telescope for dose monitoring in hadron therapy. 2014 IEEE NSS MIC.