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On the possibility utilizing nano materials and spectral imaging for holistic in-vivo cell tracking with x-rays.

In the field of regenerative medicine therapeutic approaches based on the implantation of stem cell grafts into living hosts are under development. Such therapies hold great promise for the treatment of human diseases; however results from several recent clinical studies have not shown a level of efficacy required for their use as a first-line therapy [1]. This is due to the fact that in most of these studies the fate of the transplanted cells is unknown. Thus monitoring the real-time fate of in-vivo transplanted cells is essential to validate the full potential of stem cells based therapies. Once available such real time in- vivo imaging technique would also allow localization, tracking and the characterization of the distribution of tumor cells and could be used to elucidate the knowledge of in-vivo tumor growth dynamics, which has remained difficult to obtain. At present, there are no cost effective and efficient labeling techniques for tracking cells under in-vivo conditions.
Spectral X-ray CT in combination with nanoparticulate intracellular imaging probes could be used to investigate in animal models of human diseases the location, distribution, long- term viability and preservation of functionality of implanted cells and thus help to resolve controversial issues in stem cell therapy. Moreover such technique could validate models of tumor growth in-vivo and has the potential to elucidate the role of tumor associated macrophages during decease development.
Recent studies carried out with synchrotron radiation and on µ-focus laboratory sources utilizing intracellular label methods based on phagocytosis [2,3] confirmed the feasibility of x-ray based cell tracking with single cell resolution [4] at any anatomical position in rodents. Since high resolution but low efficient x-ray imaging detectors have been employed during these trials the associated radiation dose was substantial. Utilizing solid-state pixel detectors with interpolating readout such as MOENCH [5] the associated radiation dose could be reduced by two orders of magnitudes, which would allow longitudinal investigations on an individual animal. Moreover, the inherent energy resolution of this detector would help to discriminate cell markers based on different elements.
The combination of intracellular labeling, pixel detector and µ focus source will yield a high-resolution analytical imaging tool for biomedical research and novel cell therapies. The associated project will prove and test the principle of high resolution long term cell cluster tracking in different application areas, verify its therapeutic potential, investigate possible limitations and safety risks, and determine the best conditions for its application. In this manner it will in particular advance non-invasive prediction, diagnosis, monitoring and prognosis of diseases on a holistic basis. This novel instrument will provide the necessary knowledge and know-how that helps to evaluate therapies, develop new therapies (such as new medicines and cell therapies), and plan, support, and guide therapeutic interventions.
Both, preclinical studies of tumor model progression and experimental cell therapies commonly rely on stochastic methods that involve sacrificing large numbers of animals at several key points of disease development over a period of time. The availability of the holistic real time imaging technique described here enables longitudinal, micrometric investigations of the distribution of labeled cells and subsequently the quantification of cell numbers generated from an original implant in an individual host. It could significantly improve the understanding of complex processes of disease progression and the effects of therapies. Eventually it would help to reduce the number of animals required for preclinical trials.

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