Preclinical in vivo imaging strategies to boost therapy innovation in cancer research: application to plasma

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Thanks to increasing availability of transgenic models in mice for a variety of tumours and cell lines expressing bioluminescence or fluorescence reporter genes, non invasive in vivo imaging modalities are extremely valuable tools for biomedical research, discovery and development of new therapy strategies in oncology.
Among these, biophotonic and nuclear imaging are likely the most powerful resources to quantitatively assess gene expression, specific functions, efficacy and actual delivery of a labeled drug to the target. This process can be extended to document structure/activity relationship for any therapy including drugs, radiations, microwawes, plasmas etc…

Bioluminescence is based on the non invasive detection of photons emitted by luciferase expressing cells in the living animal. This modality is a unique tool for experimental oncology and is routinely used for a variety of tumour cells to achieve screening or efficacy evaluation of new treatments. In addition to tumour burden determination with usual luciferin, specific pro- substrates that are sensitive to in vivo processing by caspases opens new perspectives for mechanistic studies based on quantitative imaging of apoptosis even for deep foci .
Near infra red fluorescence with a variety of fusion proteins for gene expression imaging and fluorochromes for labeling biomarkers is quite operational for 2D imaging and recent developments make possible to achieve reliable quantitative 3D functional or molecular explorations with great future using enzymatically activatable probes for proteases such as MMPs and Cathepsines and molecular tracers for expression of integrins and exploration of hypoxia via carbonic anhydrase IX. Examples of applications for treatments with fibered plasma (plasma gun) on orthotopically implanted tumours will be presented as well as perspectives for associated in situ examinations by fibroscopy and per-operative fluorescence imaging.

Scintigraphy and Positron Emission Tomography are clinical molecular imaging modalities with satisfactory sensitivity and quantization capabilities, even for deep sites thanks to their 3D capabilities. They offer the most reliable strategy to explore specific biomarkers for tumour proliferation, apoptosis, angiogenesis and hypoxia for the translational research in medium size animals with spontaneous cancers such as cats and dogs in order to improve predictivity of efficacy studies before to move to humans.

Due to recent technological developments, Photo Acoustic Imaging combining 3D high resolution echography to absorption of pulsed laser light by oxy and deoxyhaemoglobin is a new and very promising resource to explore tumour oxygenation. Considering the implication of Reactive Oxygen Species (ROS) in the anti-tumour activity of non thermal plasma, hypoxia is a crucial parameter that should be managed to improve plasma efficiency.