In vivo storage phosphor small animal imaging of radioarsenic labelled anti-PS antibody

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Photostimulable storage phosphor (PSP) screens were developed and introduced in the 1980s as a replacement for film/screen X-ray detection systems [1]. Today, SP technology is the key component in commercial film-less imaging systems grouped under the generic term Computed Radiography (CR). This technology is distinct from so-called Digital Radiography, where X-ray detection is digital from the moment of detection. Subsequently, SP technology was adopted by most suppliers of autoradiography equipment. While the average molecular biologist today does not have ready access to a small animal SPECT system, he or she most likely possesses or has available a SP scanner or reader that is routinely used for gel and plot applications. Compared to the standard CR reader in a radiology clinic, these scanners typically have higher spatial resolutions (down to 50 μm) and greater digital resolution (16 vs. 12 bit). Although the current trend is towards more expensive scanners that can also read direct or chemi-fluorescence assays, a multipurpose SP system can be obtained for a fraction of the cost of a minimal small animal SPECT system.

A full physical description of SP technology, including image performance parameters (MTF, NPS, DQE) can be found elsewhere [2]. In summary, the interaction of a high-energy photon with a BaF(Br,I):Eu^{2+} phosphor grain generates electrons and holes that are trapped in immediate fluorohalide matrix area. A latent image is formed in proportion to the density of the trapped carriers. Upon subsequent photostimulation using a red light source (typically a laser at 590-680 nm), the electron is liberated from its trap and recombines with a hole. The energy generated in this process is resonantly transfered to a doped Europium ion, which then decays with characteristic luminescence (390 nm). This luminescence is captured using a photomultiplier tube and digitized. With an appropriate reader, a typical SP image plate will have a linear dynamic range up to a thousand times greater than film, spanning 4-5 orders of magnitude, and reusable for tens of thousands of exposures. Due to thermal stimulation, the latent image does fade (decay constant approximately 100 minutes), so immediate reading of PSL screens is advised [3].

As described in [4], antibodies against PS (phosphatidylserine) can be used for targeting tumor endothelium. To observe pharmacokinetics over a long period of time, we labelled ch3G4 with ^{74}As ($T_{1/2}$=17.77 d) and ^{77}As ($T_{1/2}$=38 h) and recorded *in vivo* phosphor storage images daily over a period of 7 days post injection under general anaesthesia. Fig. 1 shows such pictures overlayed with X-ray images. The enrichment in the tumor is clearly visible. After 7 days a leaking of activity into surrounding tissue was observed, which was consistent with necropsy as the tumor capsule in this late stage was breaking. Biodistribution was performed at different time points [4], also matching the displayed results (c.f. Fig. 2).

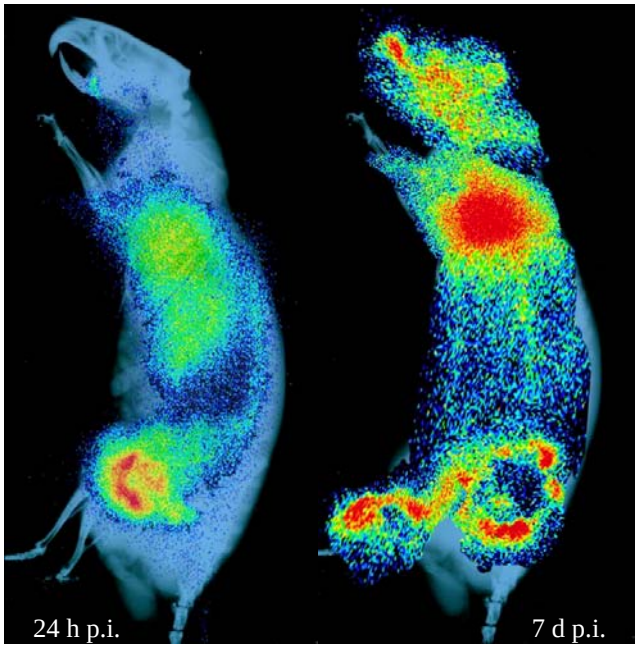

Fig. 1: small animal in vivo storage phosphor images [^{74}As]SATA-ch3G4 injected AT1 prostate tumor bearing Copenhagen rats; 24 h p.i. and 7 d p.i.

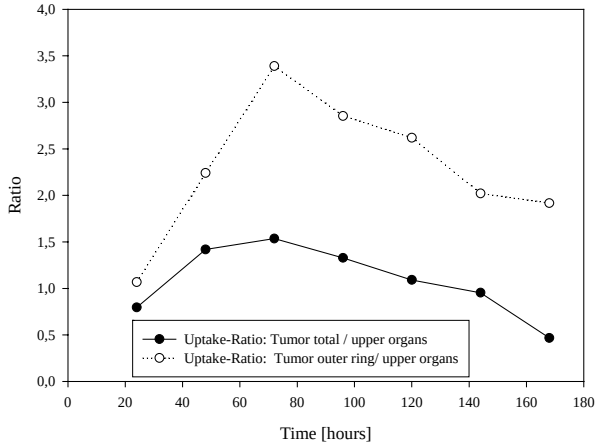

Fig. 2: pharmacokinetics of [^{74}As]SATA-ch3G4 in AT1 prostate tumor bearing Copenhagen rats followed for 7 days with *in vivo* storage phosphor technology

Conclusion: For the first time, a radioarsenic labelled antibody could be studied *in vivo* using storage phosphor technology. The anti-PS ch3G4 has a maximum tumor enrichment after 3 days and the maximum achievable activity ratio between hot spots inside the tumor and upper organs (heart, lung, liver) is 3:1.

References:

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