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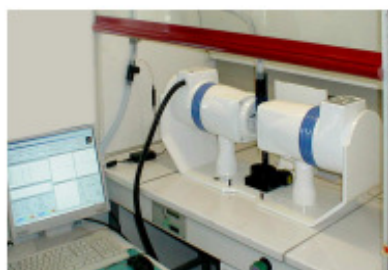
Application Notes

## In vivo SPECT imaging and quantitation of tumor angiogenesis in mice with the $\alpha\beta_3$ -specific tracer $^{99m}\text{Tc}$ -RAFT-RGD

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### Goal:

Tumor growth and metastasis are highly dependent upon neoangiogenesis. The non-invasive imaging of neovessels could therefore provide invaluable information about tumor development and treatment efficiency. Neovessels express several specific endothelial markers such as the  $\alpha\beta_3$  integrin. RAFT-RGD is a new tracer targeted at the  $\alpha\beta_3$  integrin and consisting of 4 cyclo(RGDfK) peptides bound to a cyclodecapeptide. In the present study, we sought to evaluate the potential of  $^{99m}\text{Tc}$ -labeled RAFT-RGD ( $^{99m}\text{Tc}$ -RAFT-RGD) for the non-invasive in vivo SPECT molecular imaging of neoangiogenesis using the dual-head  $\gamma$  IMAGER-S (Biospace Lab, Paris, France).



DUAL-HEAD  $\gamma$  IMAGER-S

## Material and methods:

$10^6$  syngeneic mammary adenocarcinoma (TSA) cells were injected subcutaneously in the right leg of 6 balb/c female mice (6 wks old, 20 g).

Ten days later, the animals were premedicated with an intraperitoneal injection (30  $\mu$ l) of 50% ketamine (10% wt/vol - 75 mg/kg) / 50% xylazine (2% wt/vol - 15 mg/kg) and anesthetized using isoflurane 1.5% administered through a nose cone.  $\sim 37$  MBq of  $^{99m}\text{Tc}$  RAFT-RGD were injected in a tail lateral vein, and whole-body *in vivo* SPECT image acquisition was performed for 30 min at 60 min following the injection of the tracer using the dual-head  $\gamma$  IMAGER-S. The animals were then deeply anesthetized and euthanized through cervical dislocation. The main organs were quickly removed, rinsed in saline, weighted, and tracer tissue activity was measured using gamma-well counting.  $^{99m}\text{Tc}$ -RAFT-RGD organ uptake was expressed as percentage of the injected dose per gram of wet weight (%ID/g) or as percent of the injected dose (%ID) for comparison with values obtained from quantitation of *in vivo* acquired SPECT images.

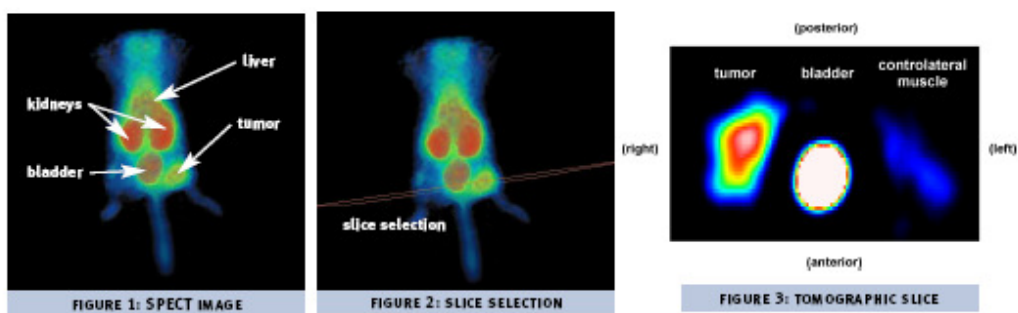
## Results :

Tumor imaging was successfully performed in all animals. A representative whole-body tomographic image of a tumor-bearing mouse injected with  $^{99m}\text{Tc}$ -RAFT-RGD is shown in figure 1.

As can be noted from the image, the tracer was mainly excreted by the kidneys and to a lesser extent by the liver. These observations were confirmed by post-mortem evaluation of  $^{99m}\text{Tc}$ -RAFT-RGD biodistribution (kidney activity, 43.2 % injected dose /g [%ID/g] ; liver activity, 7.5 %ID/g).

Image quantitation was performed:

- on a two-dimensional axial slice selected from whole-body SPECT images and comprising the tumor as well as the controlateral muscle (see figures 2 and 3).



The tumor-to-controlateral muscle activity ratio computed using  $\gamma$  VISION + software reached 5.7. This value was in agreement with that calculated from the biodistribution data (tumor activity, 4.5 %ID/g; muscle activity, 0.8 %ID/g, tumor-to-muscle ratio, 5.3).

- on 3D volumes of interest selected from *in vivo* acquired three-dimensional SPECT images :

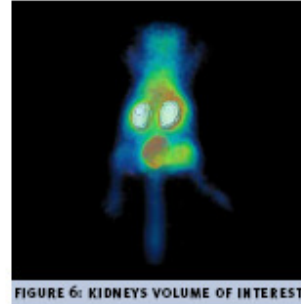
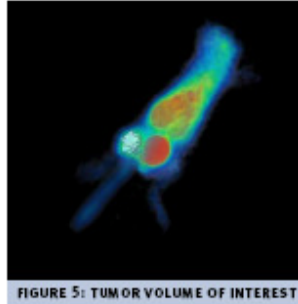
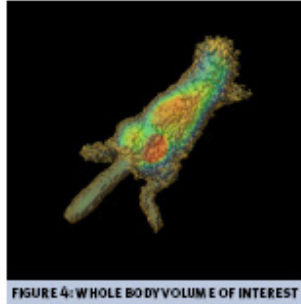


Image quantitation of  $^{99m}\text{Tc}$ -RAFT-RGD activity in the kidneys and in the tumor from *in vivo* acquired  $\gamma$  IMAGER-S three-dimensional SPECT images (11.1% ID and 1.4% ID, respectively) were correlated to those observed from post-mortem biodistribution studies (10.8 % ID and 1.5 % ID, respectively).

### Conclusion :

The sensitivity and resolution of the dual-head  $\gamma$  IMAGER-S permitted the non invasive tomographic molecular imaging of  $\alpha\beta_3$  expression with  $^{99m}\text{Tc}$ -RAFT-RGD as well as the determination of the relative *in vivo* biodistribution of the tracer in a mouse model of tumor angiogenesis. These measurements have been performed using tomographic slices and 3D volumes of interest.



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