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Small animal model in the development of radiopharmaceuticals - the step forward to clinical studies

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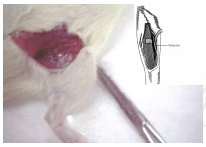
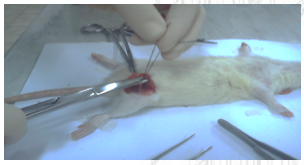
Why introduce and use small animal in the development of new drugs including radiopharmaceuticals

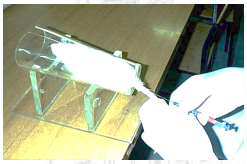
- To contribute substantially for the better understanding of mechanisms of disease
- To show the novel approaches in imaging and image analysis were equally important to meet the challenges of analyzing the complex mechanisms underlying pathophysiological processes in vivo.
- Biodistribution and pharmacokinetics studies diagnostic or therapeutic radiopharmaceuticals by SPECT or PET imaging followed by *post mortem* analysis in diseases model gives a good start point for further steps toward clinical applications

Our work in experimentally designed animal models as an essential part in the development of new radiopharmaceutical products for diagnostic and therapeutical purpose:

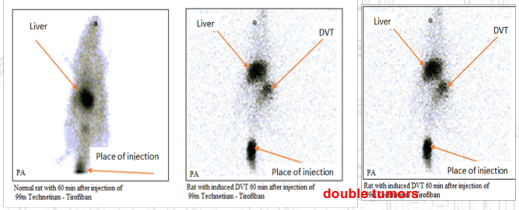
Animal model on RATS - *Wistar*







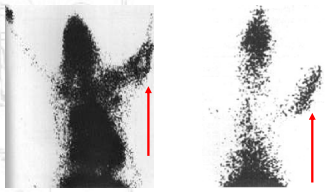
99mTechnetium- Tirofiban / **GPIIb/IIIa inhibitor** ***– imaging of*** **stasis-induced thrombus in the femoral vein after injection of thrombin to demonstrate deep venous thrombosis**



double tumors

99mTechnetium- human IgG– imaging of

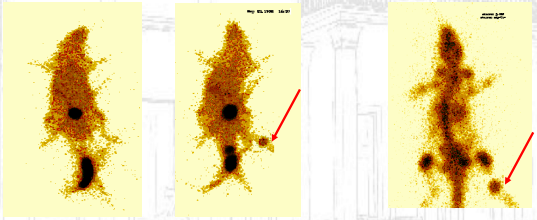
bacterial abscesses by the injection of *Staphylococcus aureus* by multiple intradermal injections



24 after administration

48 after administration

99mTechnetium-beta2 microglobulin – imaging of **deposit in the osteoaricular tissues in dialysis related amyloidosis induced by multiple i.v. application of beta 2 - microglobulin**



Normal scintigraphy with 99mTc–beta2 microglobulin

Indused amyloidosis scintigraphy with 99mTc–beta2 microglobulin

Indused amyloidosis scintigraphy with 99mTc–beta2 macroglobulin and 99mTc-MDP (bone deposits)

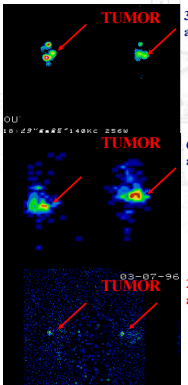
Chemical induce Croh'n disease to tested orally administrated gelatin microspheres containing 131 Iodine - Chitosan

24 after administration

48 after administration

Animal model on MICE – nu/nu – *NUDE*

99mTechnetium radiolabeled bispecific antibodies Two-step pretargeted immunoscintigraphy



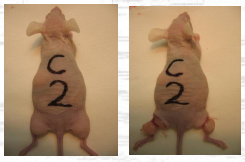
3 h after application

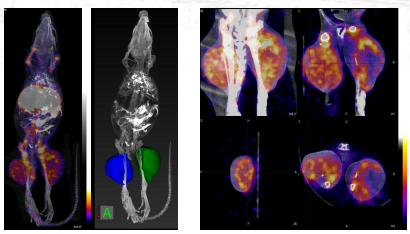
6 h after application

24 h after application

LS174T tumor-bearing mouse imaged with the gamma camera at selected time after injection of 99mTc-AG8
The mouse was given a preinjection 24h earlier of antiHSG-antiCEA antibody

177-Lutetium conjugated antibody / Rituximab - Imaging of double toumor



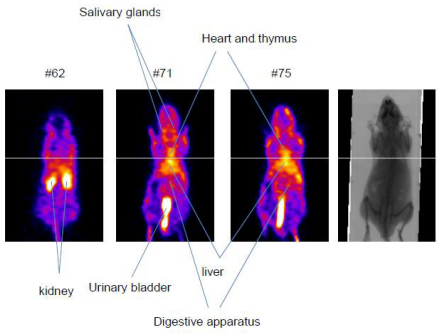


SPECT/CT imaging

PET/MRI imaging

Animal model on MICE – *BALB/c*

99mTechnetium / 188 Rhenium - Substance P – imaging of normal mice distribution



Key points:

- ❖ The use of experimental animal models in the design of new drugs including radiopharmaceuticals is a key part of preclinical trials.
- ❖ This approach can not fully replicate human disease or the varied and complex physical and psychological manifestations of human conditions.
- ❖ The process of experimental design should be carried out routinely to ensure the generation of valid, reproducible and published data.