DEEP LEARNING FOR IMAGE-TO-IMAGE TRANSLATION IN PRE-CLINICAL STUDIES

GLOTSOS DIMITRIS

dimglo@uniwa.gr

Medical Image and Signal Processing Lab (MEDISP)

Department of Biomedical Engineering

University of West Attica

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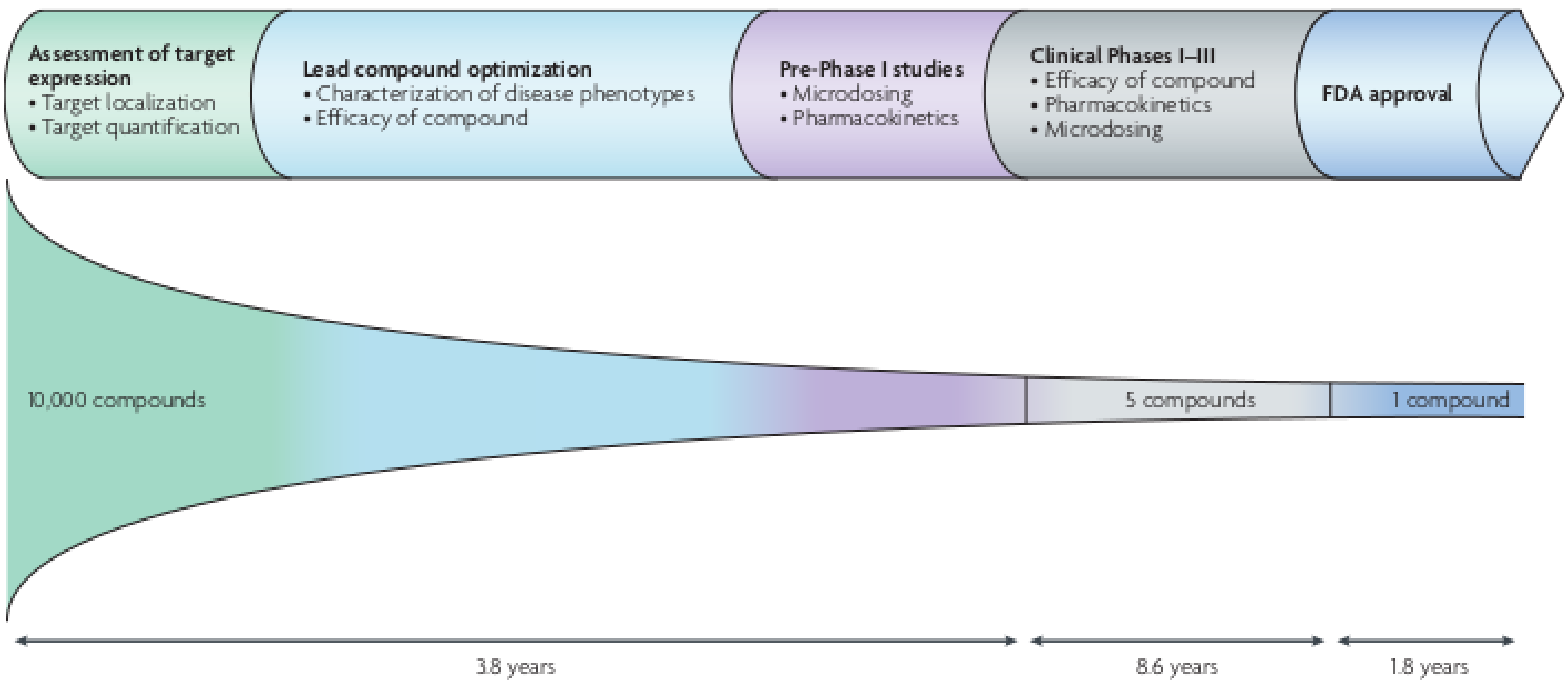
PRE-CLINICAL RESEARCH

Introduction

- Only 1 out of 10.000 candidate biomolecules will be approved as a drug after ~15 years
- Studies are conducted by thousand small and medium research groups/companies



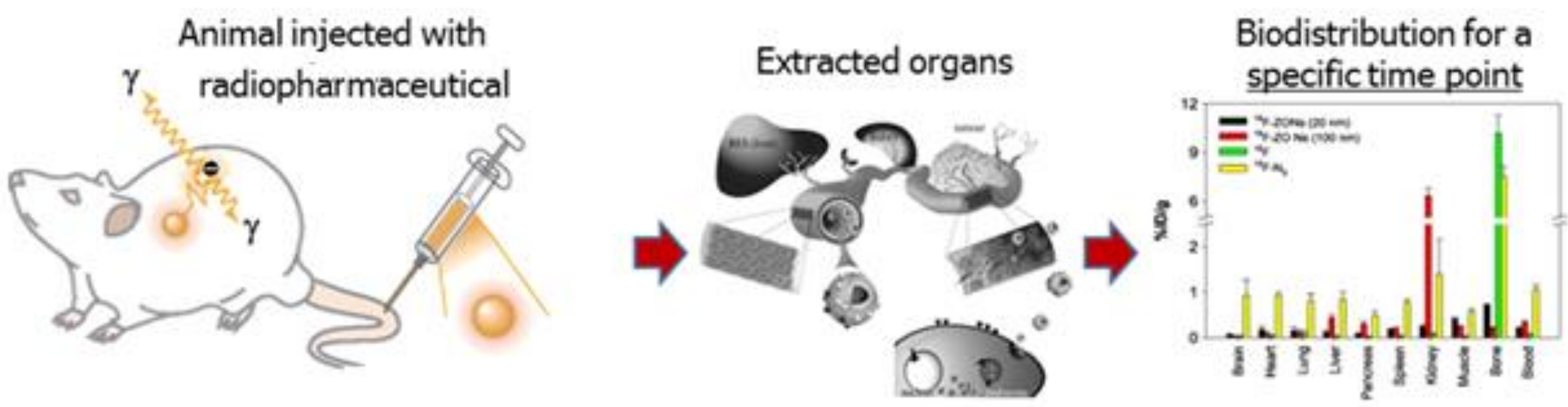
Willmann, J. K., van Bruggen, N., Dinkelborg, L. M., & Gambhir, S. S. (2008). Molecular imaging in drug development. Nature Reviews Drug Discovery, 7(7), 591–607. doi:10.1038/nrd2290

PRE-CLINICAL RESEARCH

Introduction

- Biodistribution studies

- Large number of animals required
- Cost to purchase/maintain them
- Long time to process data



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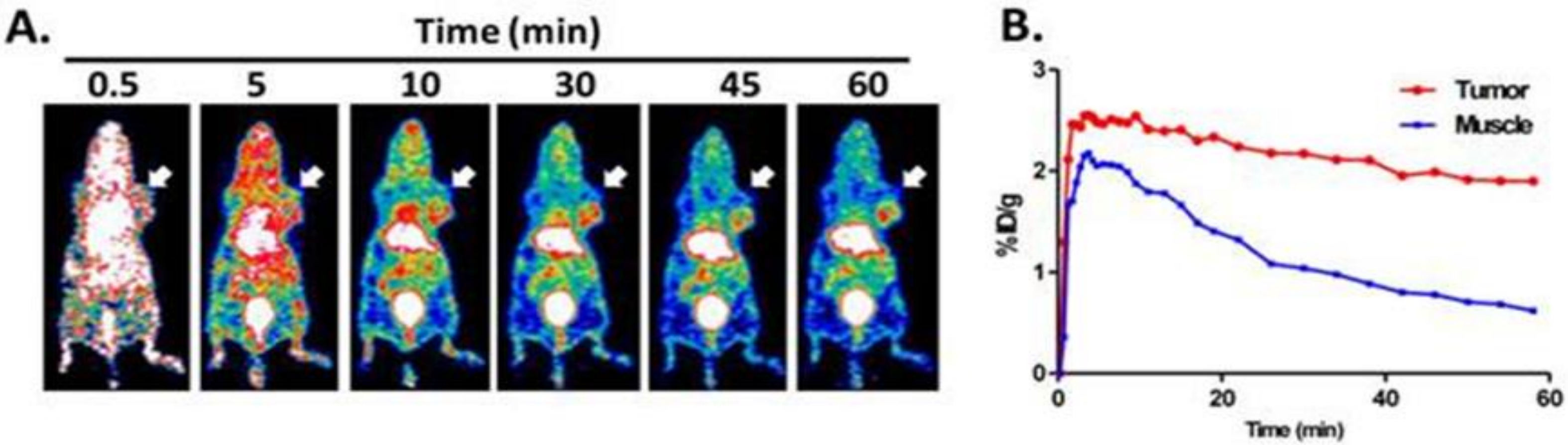
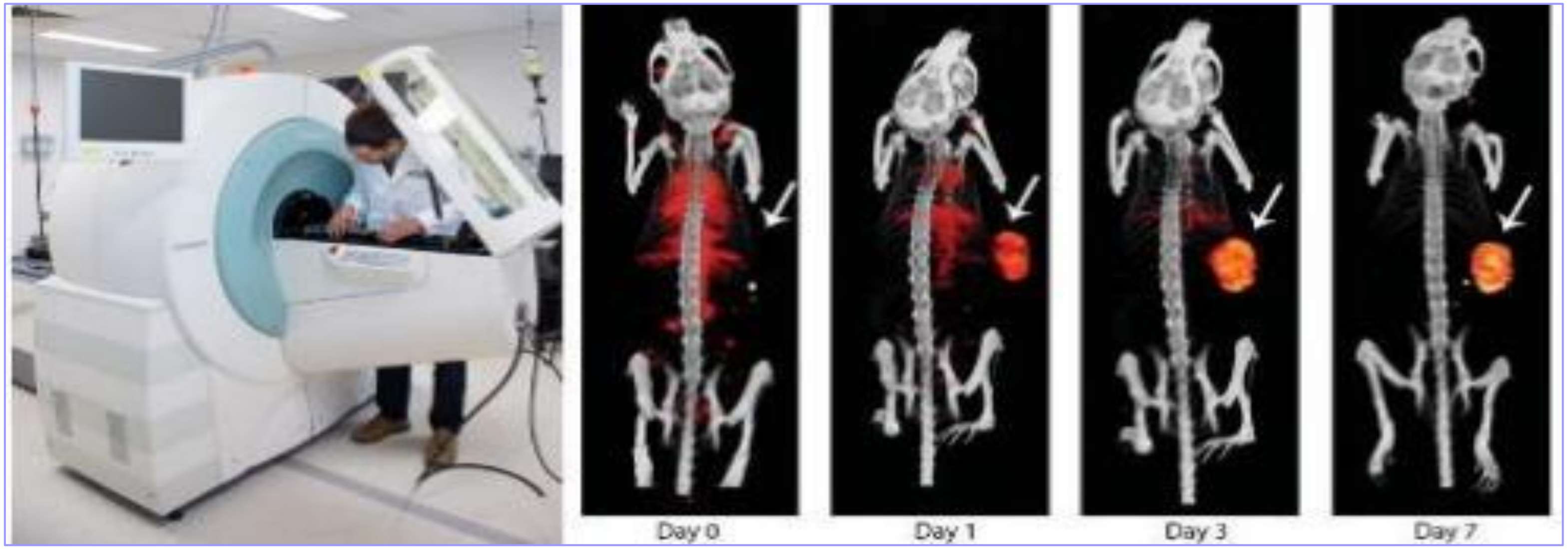


PRE-CLINICAL RESEARCH

Introduction

- Tomographic studies

- High performance
- Have high cost (>500κ€); not affordable for most of the researchers
- The size, weight, complexity in use and service contract introduce further restrictions

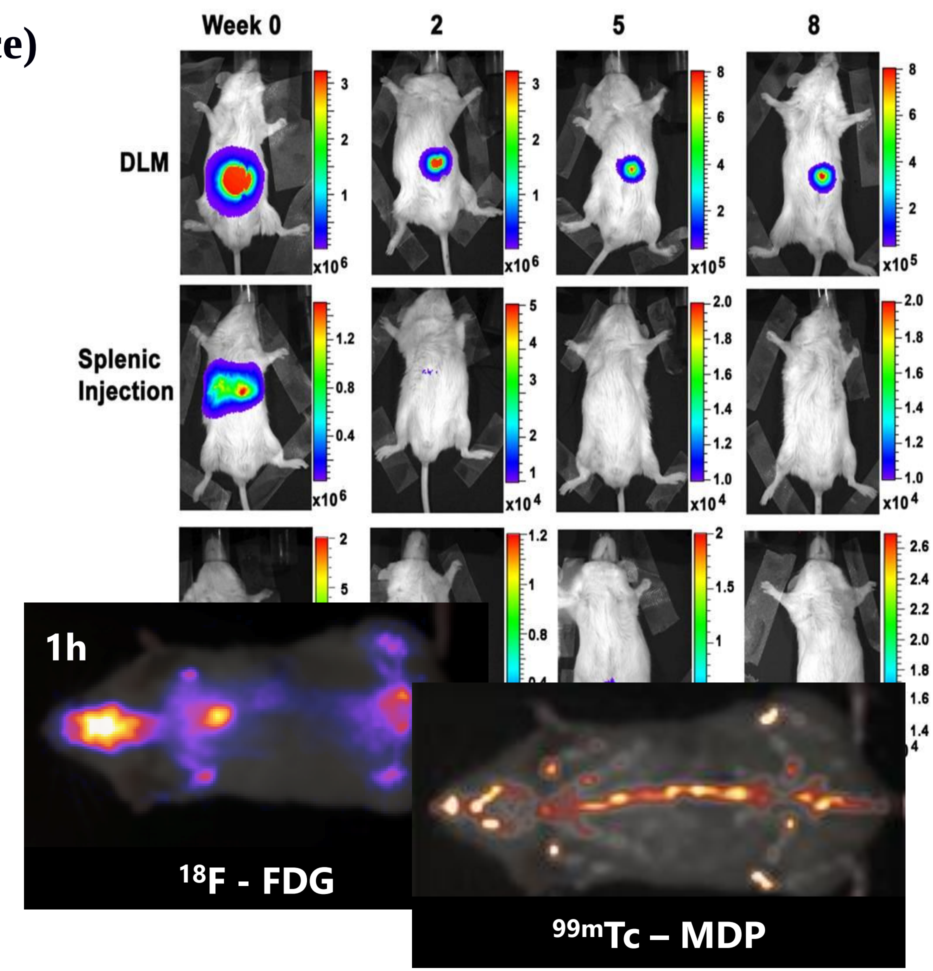


PRE-CLINICAL RESEARCH

Alternatives

- Planar imaging (Radioisotope / Fluorescence)

- Fast screening
- Cost similar to other radiochemical equipment
- High performance and competitive cost

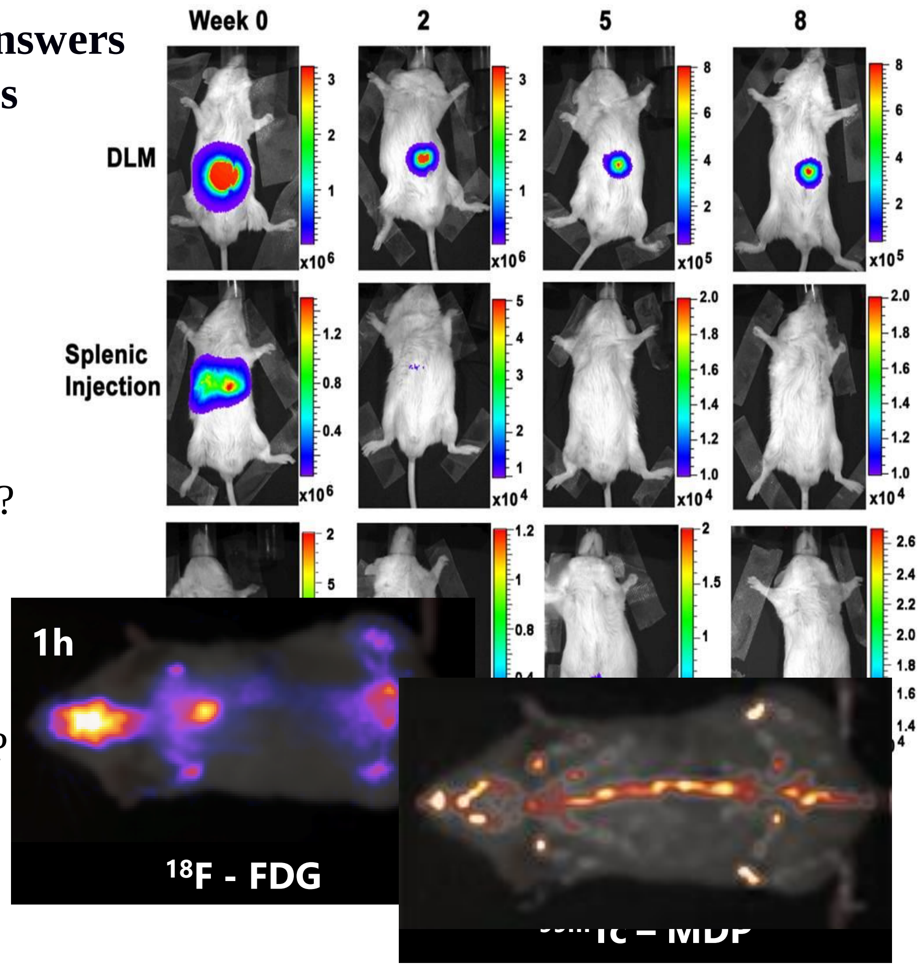


PRE-CLINICAL RESEARCH

Alternatives

- In vivo planar molecular imaging – giving answers to questions when studying new biomolecubes

- Do biomolecules reach the target?
- Are they concentrated in other organs/tissues?
- How long do they remain on the target?
- How long do they stay in blood circulation?
- Are they stable post injection?
- What happens at the first minutes post injection?
- What is the best injected concentration?
- When is the highest concentration in target?
- When is the best time point for Tomography?
- When is the best time for biodistribution points?



OBJECTIVE OF THE STUDY

Goal

- Translation of a photographic mouse image to an X-ray scan
- How? *Using a conventional image sensor and deep learning techniques*
- Why? *To combine 2D functional imaging signals with useful localization information*
- Artificially X-ray will not be used for diagnosis, only for preliminary anatomical mapping

Photographic image

X-ray image

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Photographic image

Deep learning
pix2pix

X-ray image

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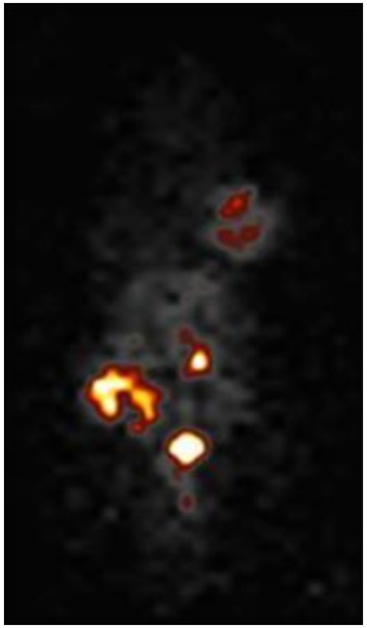
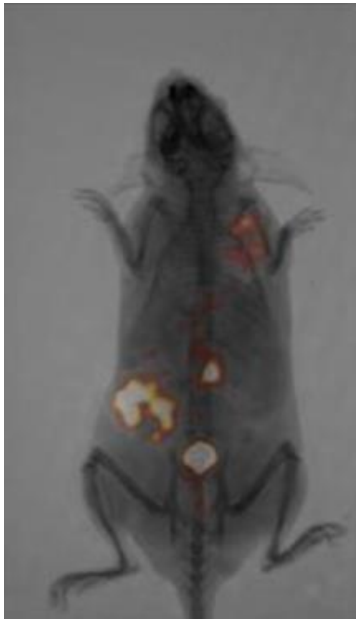
X-ray image



Scintigraphy image



Hybrid image

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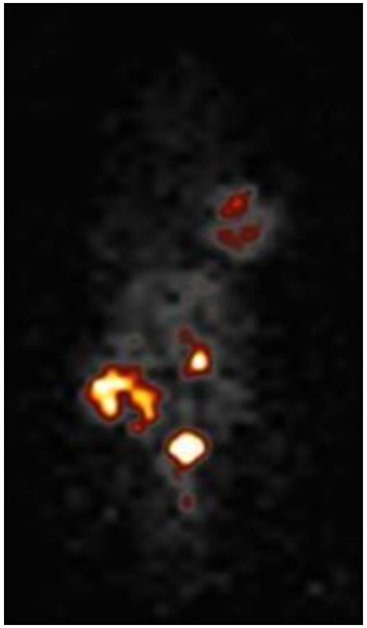
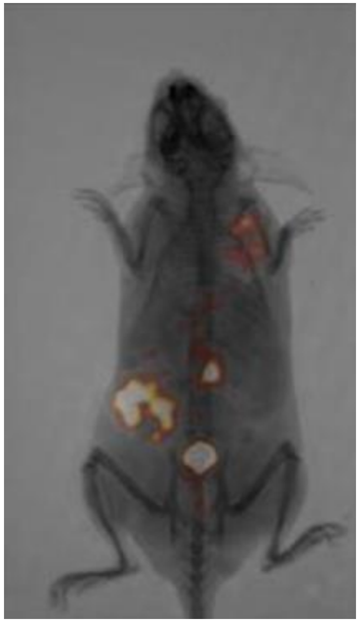
X-ray image



Scintigraphy image



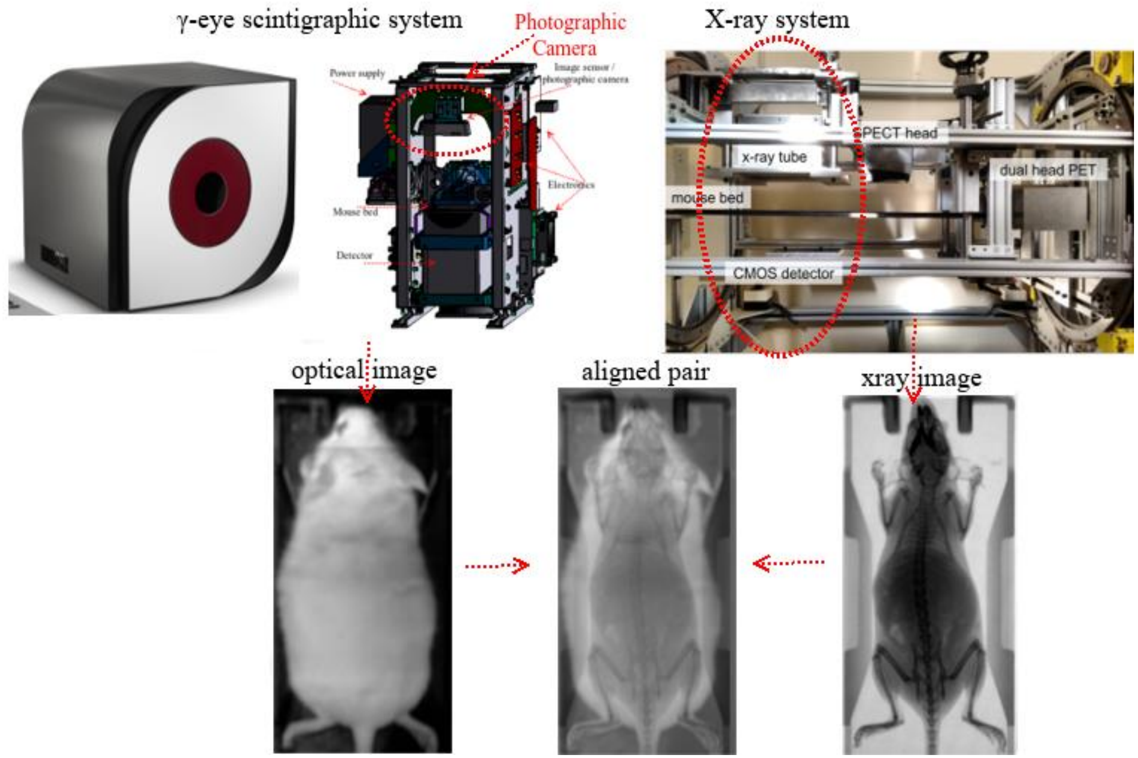
Hybrid image

METHODOLOGY

Approach and modelling

Mouse photographic image:

- γ-eye: In vivo planar scintigraphic imager for SPECT isotopes (BIOEMTECH, Athens)
- Contains a simple photographic sensor to provide a static optical image of the animal



Mouse Xray scan (ground truth)

- x-ray tube (Source-Ray Inc, US) and CMOS detector (C10900D, Hamamatsu, Japan), mounted on a rotating Gantry

- **Both systems are optimized for small mice imaging providing a field of view of 50 mm×100mm.**

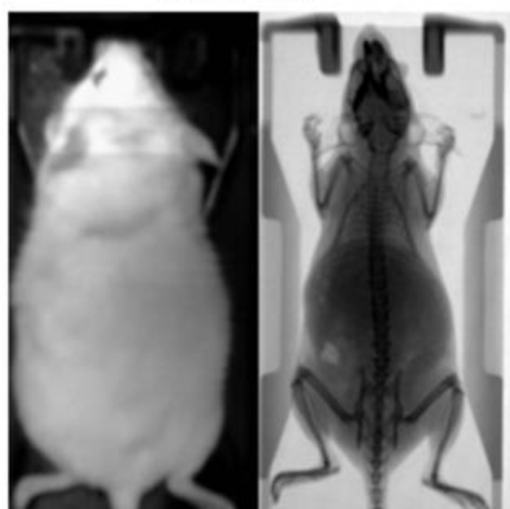
METHODOLOGY

Data collection

- 780 input/output images, 78 black mice και 78 white mice (512 × 1024 pixels)
- 5 paired images for each animal by placing it in 5 different poses upon the hosting bed
- Small mice used in molecular imaging studies have similar dimensions and weight

acrylic bed / white mouse
no cover

plastic bed / white mouse
no cover



plastic bed / black mouse
with cover

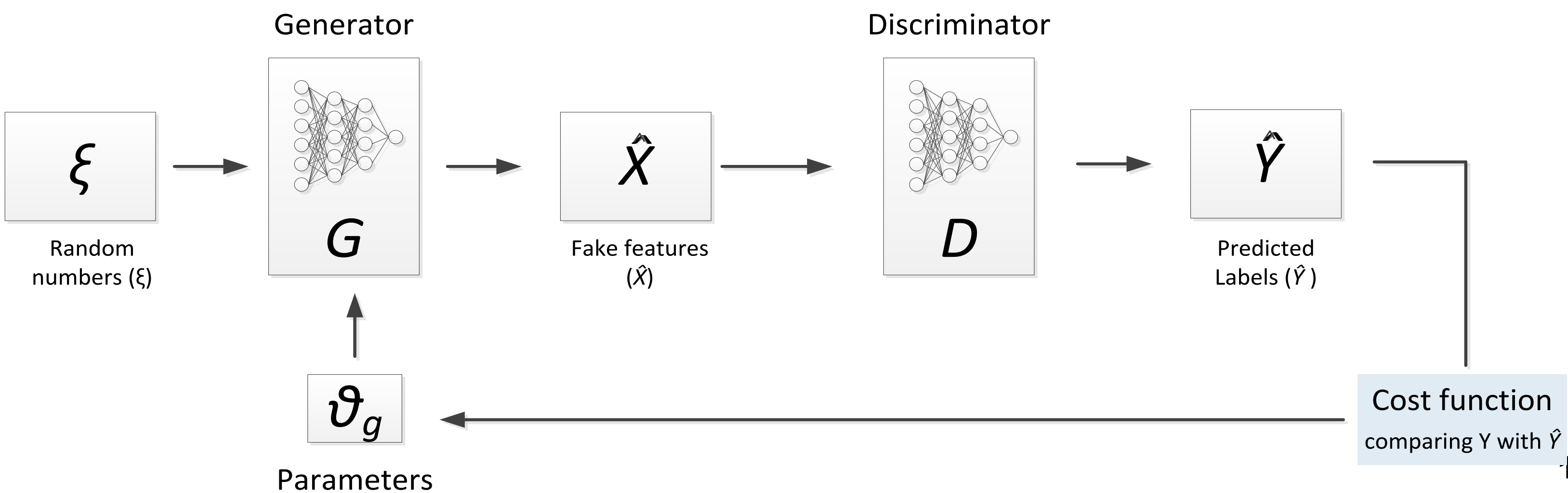
METHODOLOGY

Approach and modelling

- Off-the-shelf approach - translation of a photographic mouse image to an X-ray scan
- Image-to-image translation using pix2pix network.
- cGAN learns a mapping from the input photographic mouse image and a random noise vector to an output X-ray image.
- It comprises of two main sub-networks, the generator and the discriminator

Generator

Isola, P. et al., Image-to-image translation with conditional adversarial networks., CVPR, 2017



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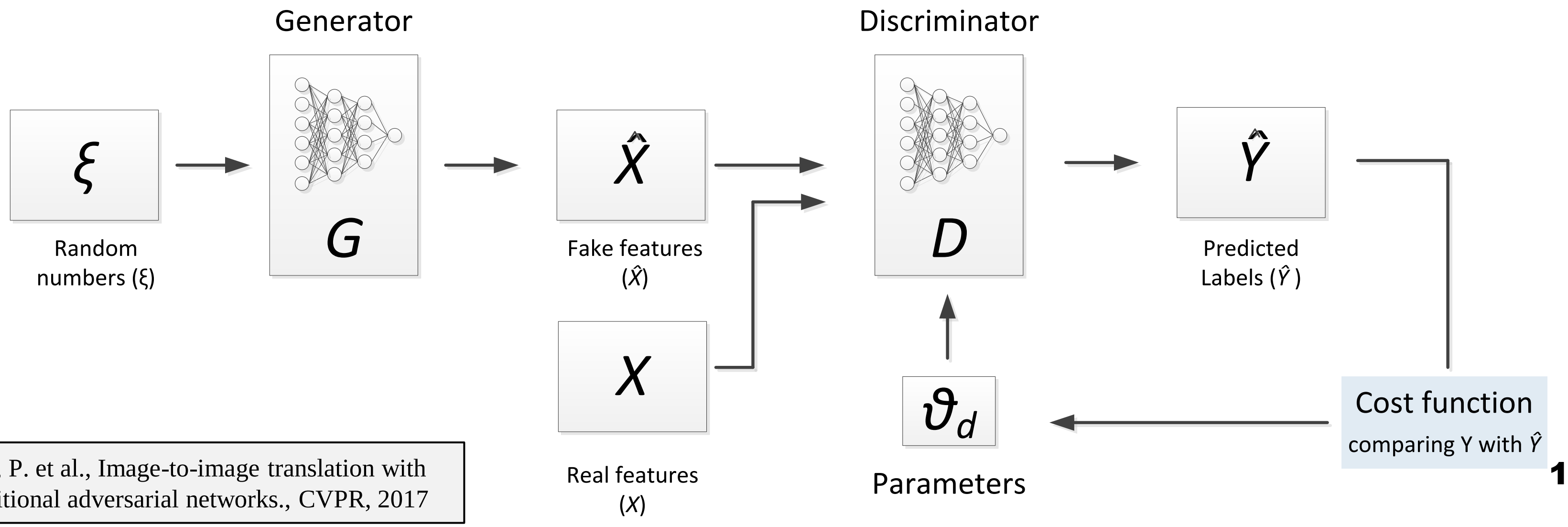
Discriminator



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METHODOLOGY

Approach and modelling

- **Three different loss functions were evaluated:**

a) cross entropy, b) Mean square error (MSE), c) Wasserstein distance

- **Three different metrics were used to evaluate the quality of the fake images:**

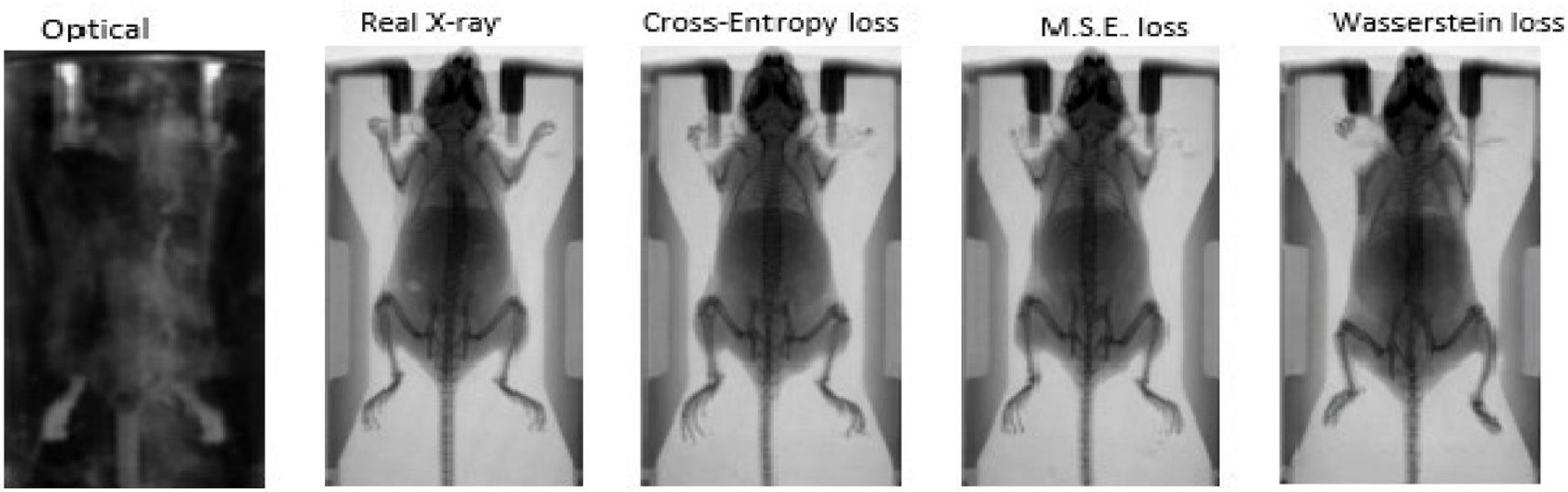
a) peak signal-to-noise ratio (PSNR), b) structural similarity index measure (SSIM), c) Frechet inception distance (FID)

RESULTS

Fake x-ray image production, evaluation

- Indicative optical to X-ray translations in the test dataset for the four distinct combinations of mouse and bed color that the pix2pix network has been trained on
- Quantitative evaluation of network outputs compared to ground truth images has been performed using three performance metrics: (a) PSNR; (b) SSIM; (c) FID

CGAN Loss Function	PSNR	SSIM	FID
Cross entropy	21.923	0.771	85.428
MSE	21.954	0.770	90.824
Wasserstein distance	17.952	0.682	162.015



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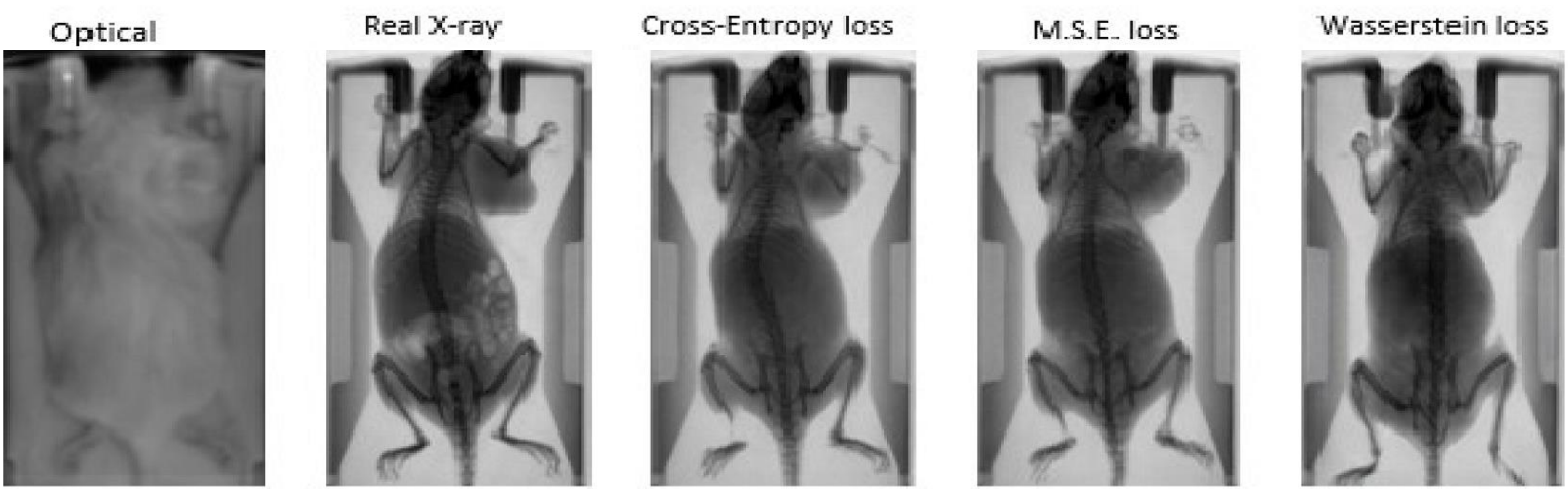
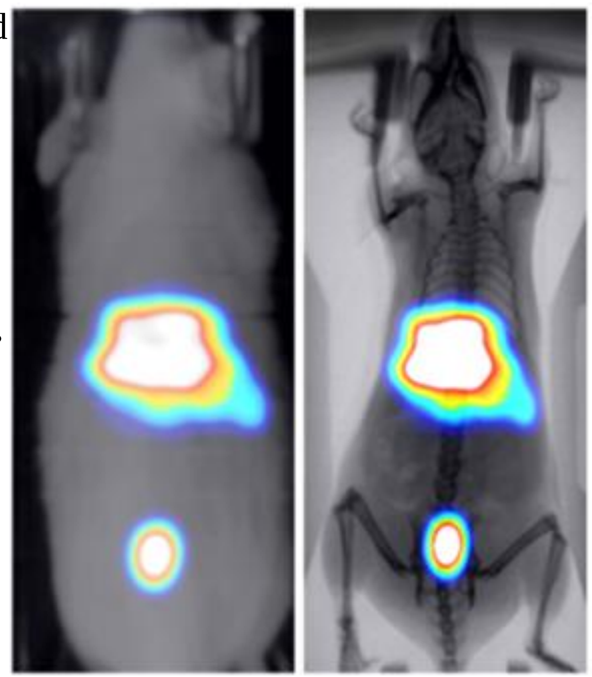


RESULTS

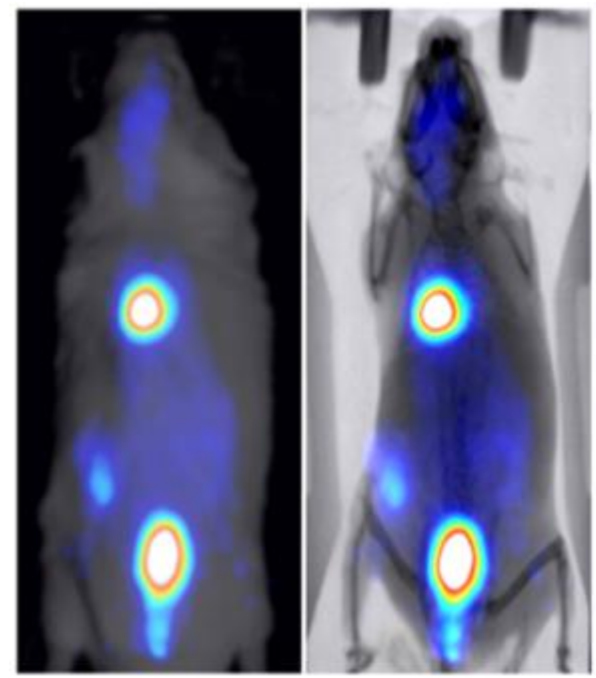
Scintigraphy experiments with mice

The proposed trained network was used for anatomical mouse mapping in three proof of concept, nuclear molecular imaging experiments

- Two healthy mice were administered through tail vein injection
- *99mTc - MDP, γ-eye scintigraphic system (BIOEMTECH, Athens) / Planar screening of SPECT isotopes*
- *18F-FDG, β-eye planar coincidence system (BIOEMTECH, Athens) / Planar screening of PET isotopes*
- Nuclear images show the expected biodistribution of the compounds in the healthy mice.\
- The produced X-ray provides the anatomical map of the small animal enhancing the overall image information.



99mTc-MDP, healthy mice, γ-eye SPECT



18F-FDG, healthy mice, β-eye PET

RESULTS

Scintigraphy experiments with mice

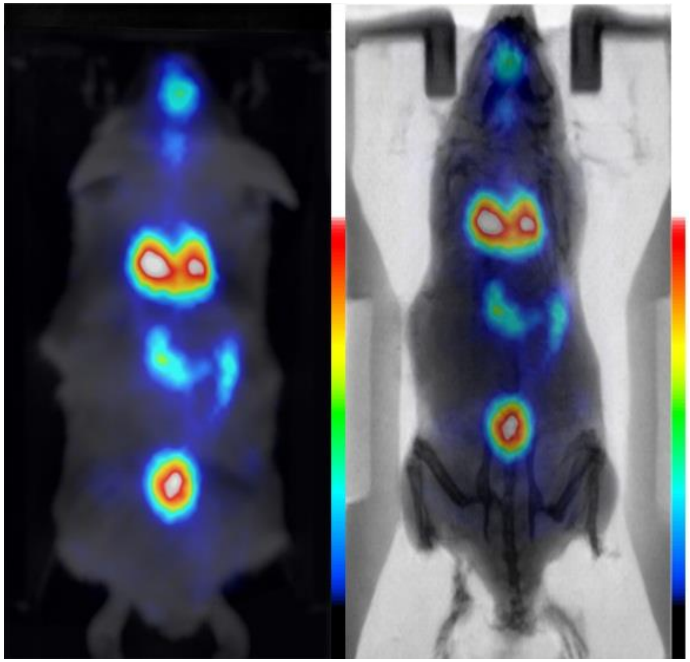
The proposed trained network was used for anatomical mouse mapping in three proof of concept, nuclear molecular imaging experiments

•Unhealthy mouse administered through lung installation

•*99mTc - MDP, γ-eye scintigraphic system (BIOEMTECH, Athens) / Planar screening of SPECT isotopes*

•Nuclear image shows clear targeting of the compound and the biodistribution in kidneys and tumor, as main organs of accumulation.

•The produced X-ray provides the anatomical map of the small animal enhancing the overall image information.



99mTc-MDP, unhealthy mouce,
γ-eye SPECT

ACKNOWLEDGEMENTS

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Research team:

Eleftherios Fysikopoulos[1], Maritina Rouchota[1], Vasilis Eleftheriadis[2], Christina-Anna Gatsiou[2], Irinaios Pilatis[2], Sophia Sarpaki[2], George Loudos[1], Spiros Kostopoulos[1] and Dimitrios Glotsos[1]

[1] Biomedical Engineering Department, University of West Attica, Athens, Greece

[2] Bioemission Technology Solutions (BIOEMTECH), Lefkippos Attica Technology Park, N.C.S.R Democritos, Athens, Greece