Pre-clinical and clinical dosimetry in internal radiation therapy and imaging

OpenGATE meeting – Clermont-Ferrand – 11-12 May, 2017

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Overview

- Internal dose estimates using MIRD method: general view
- Preclinical and clinical studies performed at LPC:
  - [^{177}Lu]DOTA-Ts29.2 in RIT of colorectal cancer
  - [^{131}I]ICF01012 in TRT for melanoma treatment
  - ^{99m}Tc-NTP 15-5 for cartilage imaging in arthrosis related pathologies
- Dosimetry calculations using GATE
- Future developments

Introduction

DOSE = Cumulated Activity $\times$ S-factor

Cumulated activity: is represented by the area under the time activity curve $\tilde{A} = \int_0^\infty A(t)dt$

ACTIVITY DISTRIBUTION:
- bio-distribution by organ harvesting;
- SPECT-CT imaging after radiotracer injection.

S-factor: is the mean absorbed dose in the target per nuclear transformations in the source
It is calculated by GATE Monte Carlo simulations.

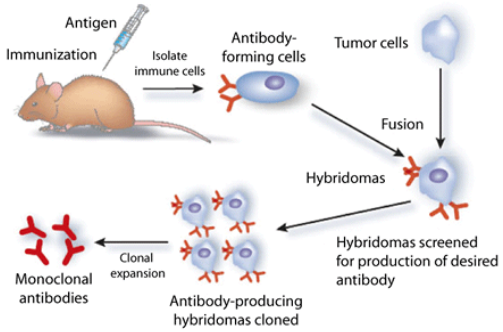
[^{177}Lu]DOTA-Ts29.2

RIT (RadioImmunoTherapy)

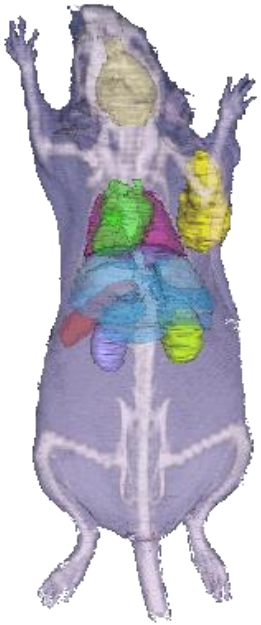
Ts29.2 is a murine monoclonal antibody specific for human tetraspanin-8 (TSPAN8)

TSPAN8 gene is overexpressed in human colorectal cancer (CRC)

→ Targeting TSPAN8 in CRC with radiolabeled Ts29.2



Dosimetry in pre-clinical trials:
mouse model obtained from segmented CT-scan
The ratio of absorbed doses in the tumor to non-targeted organs was evaluated



Publication:

www.impactjournals.com/oncotarget/ Oncotarget, Advance Publications 2017

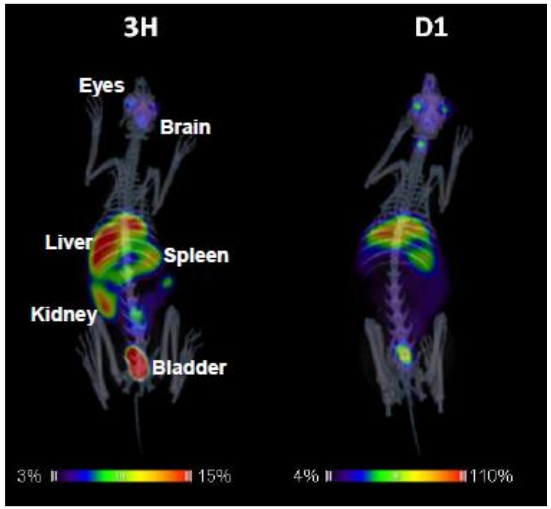
Tetraspanin 8 (TSPAN 8) as a potential target for radio-immunotherapy of colorectal cancer

Aurelie Maisonial-Besset[1,2,*,**], Tiffany Witkowski[1,2,*,**], Isabelle Navarro-Teulon[3,4,5], Odile Berthier-Vergnes[6,7], Giovanna Fois[2,8], Yingying Zhu[9,10,11], Sophie Besse[1,2], Olivia Bawa[12], Arnaud Briat[1,2], Mercedes Quintana[1,2], Alexandre Pichard[3,4,5], Mathilde Bonnet[2,13], Eric Rubinstein[9,10,11], Jean-Pierre Pouget[3,4,5], Paule Opolon[12], Lydia Maigne[2,8], Elisabeth Miot-Noirault[1,2], Jean-Michel Chezal[1,2], Claude Boucheix[9,10,11,*], Françoise Degoul[1,2,*]

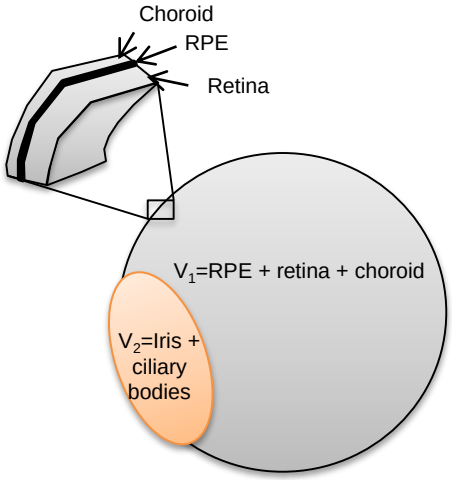
[^{131}I]ICF01012

Radionuclide Therapy:

- ICF01012 is a melanin ligand
- Melanin targeting is of interest for the treatment of disseminated melanoma
- Time activity data: SPECT-CT imaging and Bio-distribution experiments
- S values calculated through GATE simulations



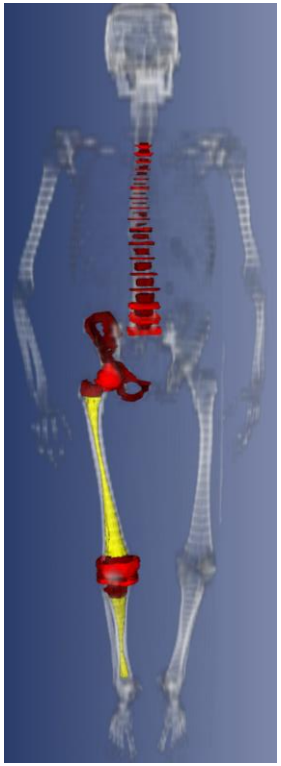
- ➢ Extrapolation to human
- ➢ Detailed study for eyes



Manuscript submitted for publication to PMB
"**Radiation dosimetry of [131I]ICF01012 in rabbits: application to targeted radionuclide therapy for human melanoma treatment**"
E.Jouberton, Y.Perrot, B.Dirat, T.Billoux, P.Auzeloux, P.Labarre, J-M.Chezal, C.Valla, M.Filaire, A.Vidal, C.Millardet, E.Miot-Noirault, F.Cachin, L.Maigne, F.Degoul

^{99m}Tc-NTP 15-5

- Validation of a molecular imaging targeting cartilage proteoglycans
- Dosimetry profile associated to ^{99m}Tc-NTP 15-5 imaging of cartilage
- Activity distribution: organ sampling from rabbits
- S-factors values calculated from rabbit CT-scan and human CT-scan → toward clinical trials



GATE calculation using Split Exponential Track Length Estimator (seTLE)

→ a first efficiency study showed a 210 increase in efficiency using seTLE

Talk accepted for AAPM meeting, Denver 2017
"Dosimetry study of ^{99m}Tc-NTP 15-5 imaging of cartilage in preclinical trials using the GATE Monte Carlo platform"
G.R.Fois, E.Jouberton, C.Valla, N.Sas, F.Cachin, E.Miot-Noirault, L.Maigne

Poster accepted for AAPM meeting, Denver 2017
"Implementation of S-factor calculation for personalized radionuclide therapy dosimetry into the GATE platform"
G.R.Fois, F.Smekens, L.Maigne

Internal dosimetry procedure: S-factor calculation with GATE

OUR PROCEDURE:

1) Creation of a DICOM-RT file with contoured images from CT scan:

DICOM-RT: extension applied to radiation therapy

RT Structure set: defines areas of significance (such as TV, OAR, body contours, ecc.)

ROI Contour: contains contours vertices coordinates.

2) From vertices coordinates of the contour we build a binary mask

Analyze format: header .hdr + raw

3) Simulation in GATE

Geometry ⟶ Nested parametrization method

Source ⟶ Voxelized source

GATE OUTPUT : S-factors for our geometries *[absorbed dose per unit cumulated activity]*

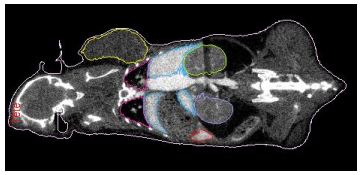
Summary and future perspectives

IDEA/GOAL: simplify internal dosimetry calculations in GATE

potential users: *- radiation protection of patients during nuclear medicine diagnostic procedures ;*
- dosimetry in treatment using radionuclide therapy ;
- new radiopharmaceuticals for diagnosis and treatment.

NEEDS:

- DICOM-RT



THANKS FOR YOUR ATTENTION