Dosimetry study of [^{131}I]ICF01012 in targeted radionuclide therapy of melanoma

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INTRODUCTION

Metastatic melanoma is a challenging disease to treat as it is inherently resistant to most treatments.

Melanin pigment is detected in more than 90% of primary melanomas and in 50% of metastases.

Previously, [^{131}I]ICF01012 has been evaluated in mice bearing melanomas and in healthy rabbits. Encouraging results sustain [^{131}I]ICF01012 as a good candidate for melanoma targeted radionuclide therapy (TRT) and open perspective for personalized dosimetry during phase I clinical transfer[1,2,3,4].

This study is part of the clinical trial MELRIV (NCT 03784625).

AIM

In this study, [^{131}I]ICF01012 radiopharmaceutical melanin-targeting ligand is for the first time used in patients with pigmented metastatic melanoma. We provided the associated dosimetry using the GATE Monte Carlo simulation platform[5].

Due to the high melanin concentration in retina, a great attention is dedicated to the calculation of dose in this organ at risk.

METHOD

- First, patients are selected through their response to an injection of [^{131}I]ICF01012 (185 MBq). Selection criteria are as follows : binding of [^{131}I]ICF01012 on at least a tumoral lesion and an acceptable radiation absorbed dose to major organs.
- Dosimetry is performed using the MIRD formalism.
- S-values are calculated from CT scans using the GATE Monte Carlo platform allowing a personalized dosimetry. Physics list emstandard_opt3.
- Activity distributions are obtained through SPECT-CT imaging (0.5, 1, 3, 24, 96 hours p.i.).
- Dosimetry is provided for all the detectable metastases and organs at risk: liver, kidneys, lungs, brain and retina.
- Escalation of therapeutic doses: 800-4000 MBq/m^2

PROCEDURE

Timeline of the study:

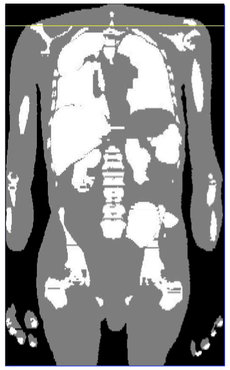
(0h-3h): A SPECT/CT scan is performed in order to select organs at risk and metastases.

(3h-4h): Anonymous CT scan and segmented organs are created in the cancer centre

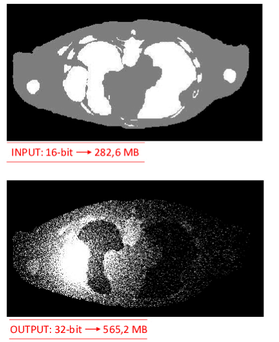
(4h-14h): S-factor calculations are performed using the GATE simulation platform over a computer cluster on 9 computing nodes each hosting 16 CPUs.

- A total number of 13 organs are taken into account: retina left, brain, lung left and right, kidney left and right, liver and spleen. 5 metastases are considered.

- Up to 10^8 primaries are simulated for every organ sources, leading to an uncertainty less than 1% for self S-values. Every source simulation is split in 10 jobs on the cluster.



Segmented organs from the patient CT scan.
Image dimensions: 512x512x539 voxels 0.9766x0.9766x3 mm^3

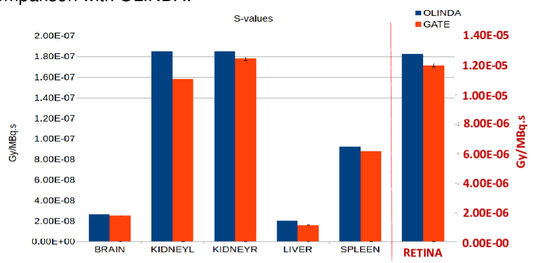


INPUT image: Segmented organs (16-bit file)
OUTPUT image: Dose maps from the GATE platform (32-bit file)
**Image of the biggest metastasis*

RESULTS

Up to 100 jobs (equivalent to 10 sources) have ran simultaneously on the computing cluster.
The running time per job was between 3 and 5 hours, so the maximum running time was 5 hours to simulate 10 organ sources.

Comparison with OLINDA:



A good agreement is shown between GATE and OLINDA software. As additional data, GATE can provide personalized results for metastases and retina.

Doses received by a patient for an injected activity activity of 1240 MBq

Doses (Gy)	
Brain	0.16
Kidney (l)	0.37
Kidney (r)	0.44
Liver	0.95
Spleen	0.25
Lung (l)	1.07
Lung (r)	1.01
Retina	1.39
Metastasis 1	5.07
Metastasis 2	0.11
Metastasis 3	6.35
Metastasis 4	7.34
Metastasis 5	1.86

CONCLUSIONS

This study shows the possibility for personalized dosimetry calculation during phase I clinical transfer using the Monte Carlo GATE simulation platform.

Personalized S-values can be obtained for up to 20 organs in less than 10 hours.

GATE will be used, following the same procedure as described, for all the patients (~30) that will be included in the clinical trial.

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5 OpenGATE Collaboration: http://www.opengatecollaboration.org/

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