Internal dose assessment of ^{177}Lu-DOTA-SP for quantification of arginine renal protection effect

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1.INTRODUCTION

^{177}Lu-DOTA-Substance P (SP) could be used in peptide receptor radionuclide therapy (PRRT) for treatment of malignant glioblastoma. The limiting factor is the dose delivered to healthy organs therefore, it is necessary to identify the organ with the highest radiological risk and calculate the maximum activity that can be administered to a patient in a safe way, it means Maximum Tolerate Activity (MTA). Because in PRRT, one the healthy organ with the highest risk of reaching radiotoxicity is commonly the kidney, in this study the results of ^{177}Lu-DOTA-SP preclinical assays carried out in NIH mice are compared and extrapolated to adult humans, for two conditions: with and without prior administration of arginine as a potential renal protective agent.

2. OBJECTIVE

To investigate the renal protective effect of arginine in the administration of ^{177}Lu-DOTA-SP in normal NIH mice and its extrapolation to standard adult patients.

3. METHODS

Biodistribution Study

~1MBq de ^{177}Lu-DOTA-SP

Injected into the tail vein of the mouse
- 20 mice in normal conditions
- 8 mice with prior administration of arginine

Sacrifice mouse at:
0.5h, 2h, 6h, 16h, 48h in normal conditions and 0.5h, 2h, 6h for mice with prior administration of arginine

Remove and weigh organs

Measure activity in automatic gamma counter

Calculate the percentage of injected activity of ^{177}Lu-DOTA-SP per gram of tissue (%IA/g)

Dosimetric Studies

Experimental data of organ activity were fitted to curves

Doses of mouse organs were determined using MIRD methodology

Extrapolation to humans was performed using time scaling method

Doses of human organs and MTA of ^{177}Lu-DOTA-SP were estimated

$$MTA\left(\frac{MBq}{Kg}\right)=\frac{Tolerance\ Dose\,(mGy)}{Dose\ Coefficients\,(mGy/MBq)\times Body\ mass}$$

4. RESULTS

Figure 1. Biodistribution data of ^{177}Lu-DOTA-SP in normal NIH mice

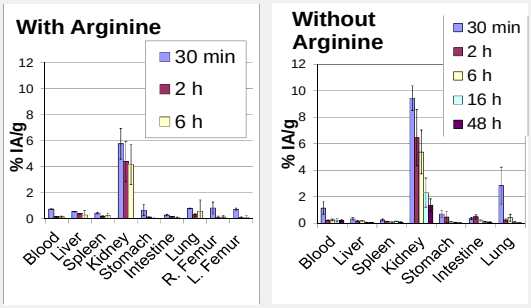

Table 1: Absorbed dose in organs of the NIH mouse (A), adult female (B) and adult male (C).

Organs	Absorbed Dose (mGy/MBq)					
	with Arginine			without Arginine		
	A	B	C	A	B	C
Kidneys	115.07	1.04	1.16	139.9	1.15	1.59
Liver	8.47	0.06	0.06	4.61	0.02	0.03
Lungs	17.05	0.02	0.02	14.57	0.06	0.05
Stomach	5.64	0.01	0.01	9.67	0.05	0.05
Spleen	27.70	0.09	0.07	14.85	0.05	0.05
Intestine	1.81	0.10	0.10	4.66	0.22	0.22
Bone Marrow	0.57	0.01	0.01	0.51	0.01	0.01

Table 2: MTA (MBq/kg) in adult humans for two cases

MTA for case with Arginine		MTA for case without Arginine	
Woman	Man	Woman	Man
338	234	306	170

5.CONCLUSIONS

Kidney is the healthy organ with the highest radiological risk, following the intravenously administration of ^{177}Lu-DOTA-SP.

It was found out that the administration of arginine prior to injection of ^{177}Lu-DOTA-SP optimize the treatment, showing a rapid clearance from the body and less retention in kidney with respect to the situation in which the amino acid is not administered.

The dosimetric results extrapolated to humans should be taken into account for not exceeding the radiotoxicological threshold in kidney (20 Gy) and thus ensure the radiological protection of patients.