Voxel based dosimetry of ^{177}Lu-PSMA-617 within a prospective clinical trial: Whole body tumour dosimetry and correlations with pre-therapeutic imaging and biochemical outcomes

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Aim: Determine the radiation dosimetry of ^{177}Lu-PSMA-617 using a voxel-based technique and analyse relationships to pre-therapeutic imaging and clinical outcomes.

Materials and methods: 30 patients with advanced prostate cancer receiving ^{177}Lu-PSMA-617 within a prospective clinical trial (ACTRN12615000912583) were studied. All patients underwent pre-therapeutic ^{68}Ga-PSMA-11 PET-CT to confirm high PSMA expression (SUVmax of tumour at least 1.5 times SUV of liver). Following therapy patients underwent quantitative SPECT-CT at 4, 24 and 96 hours. Pharmacokinetic uptake and clearance at a voxel level was calculated and cumulated activity translated into absorbed dose using Monte Carlo determined voxel S values. Volumes-of-interest were drawn on normal tissues and tumour bearing regions to determine dose. 'Whole-body' tumour dose was also defined by threshold of all tumour that received doses greater than 2 and 5 Gy. Correlations between PSMA PET-CT parameters, dosimetry and therapeutic response were analysed for spearman's *r*-values. Difference in absorbed doses to tumour in patients that achieved a PSA-response greater than 50% was evaluated by Wilcoxon-Mann-Whitney test.

Results: Mean 'whole body' tumour absorbed doses (above 2 Gy) was 7.7 Gy and (above 5 Gy) 12.55 Gy. "Whole body" tumour dose was associated with PSA response at 12 weeks with a mean dose of 14.67 Gy in patients who achieved PSA≥50% decline vs. 10.42 Gy for those achieving a PSA<50% decline ($p<0.01$). Of 11 patients receiving a tumour dose less than 10 Gy, only one achieved PSA fall ≥50% Mean absorbed dose to kidneys, submandibular and parotid glands, liver, spleen and bone marrow were 0.39, 0.44, 0.58, 0.1, 0.06 and 0.11 Gy/MBq, respectively. Tumour volume SUVmean on PSMA PET correlated with "whole body" mean absorbed dose (r=0.62). SUVmax of the parotid glands also correlated with absorbed dose (r=0.67). Absorbed dose in salivary glands was 0.65 and 0.43 Gy/MBq for the eight patients with the highest and lowest tumour burdens respectively.

Conclusions: Significant correlation between "whole body" voxel-based tumour dose and PSA response at 12 weeks was observed that could assist in identifying patients who are likely to respond based on post-treatment imaging. Patients receiving a dose less than 10 Gy were unlikely to achieve a fall in PSA≥50%. Significant correlations between aspects of screening ^{68}Ga-PET-CT and tumour and normal tissue absorbed dose were observed that might allow *a priori* prediction of response and toxicity. A reduction in salivary absorbed dose was observed in patients with higher tumour burdens providing a rationale for patient-specific dosing.

Conflicts of Interest: No authors report any relevant conflicts of interest

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