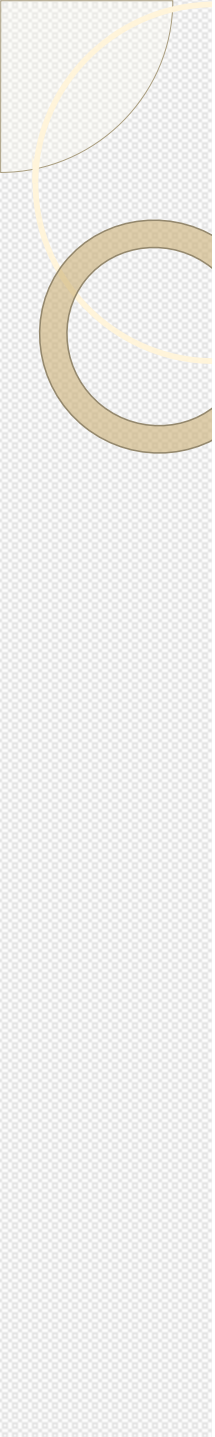


Post-tracer Dosimetry of Lu-177-DKFZ-617 Prostate Specific Membrane Antigen (PSMA) Inhibitor In patients with Castration Resistant Prostate Cancer

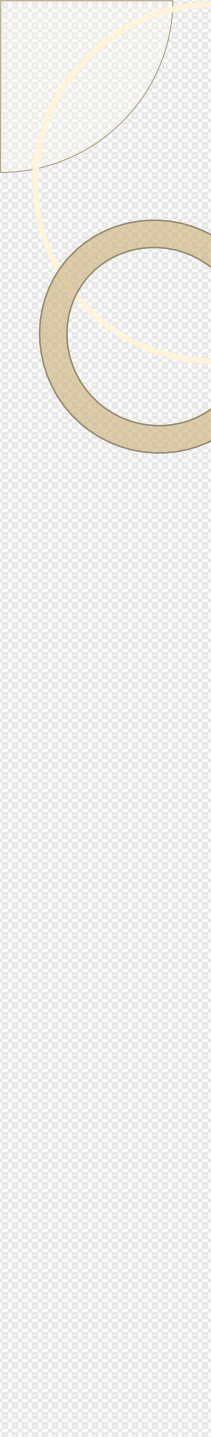
Abuqbeitah Mohammad¹, Levent Kabasakal¹, Yeyin Nami¹, Aygun Aslan¹, Demirci Emre², Ocak Meltem³, Mustafa Demir¹





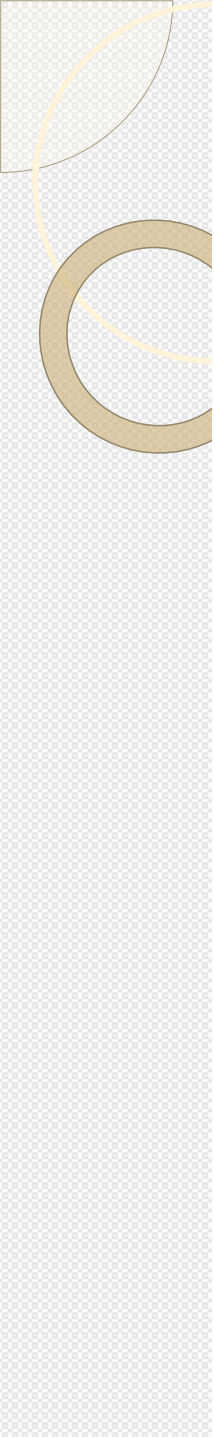
Golden Goal

- a pilot study to estimate radiation-absorbed doses to target organs in order to develop a treatment plan for the systemic therapy of Lu-177-DKFZ-617 PSMA ligand in patients with castration resistant prostate cancer.



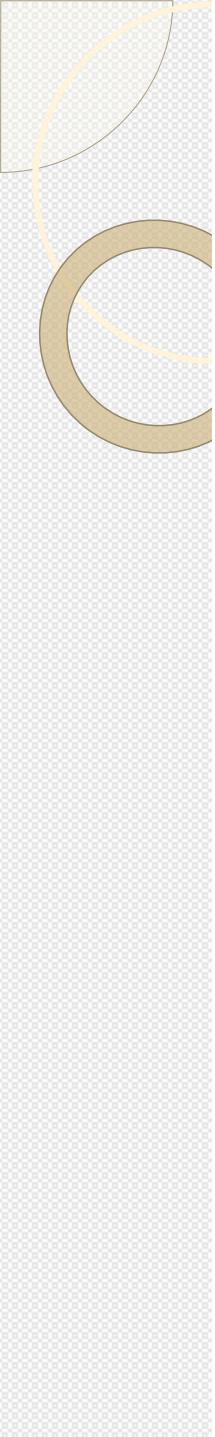
Introduction

- (PSMA) is a type II membrane glycoprotein highly expressed by all prostate cancers and the expression increases with tumor aggressiveness, metastatic disease and disease recurrence
- Glu-NH-CO-NH-Lys-[Ga-68-(HBED-CC)] (Ga-68-DKFZ-PSMA-11) has been suggested as a novel tracer that can detect prostate cancer relapses and metastases with high contrast by targeting the PSMA



Methodology

- 7 patients were included to the study
- The ages ranged from 57 to 70 years (mean 63.9 ± 3.9 years).
- Patients had prostatic surgery (n=3), radiation therapy (n=4).
- All patients had hormonal therapy and had increasing blood PSA levels. The Gleason score was 9 in 3 patients, 8 in 3 patients, 7 in 1 patient Blood PSA levels ranged from 19 to 235 ng/ml (mean 85.43 ± 74.46 ng/ml)



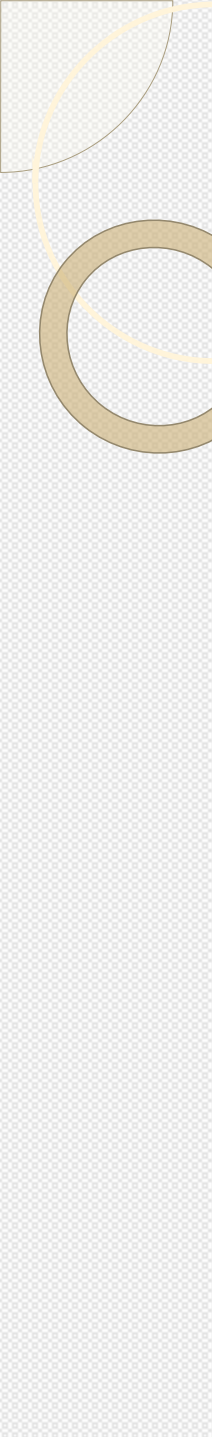
PET/CT Assessment

- After the preparation and quality control of the radiotracers all patients received 75 to 150 MBq of Ga-68-DKFZ-11 PSMA ligand intravenously. Whole body images acquired 45 to 60 min p.i. of radiotracer using an integrated PET/CT scanner

Dosimetry

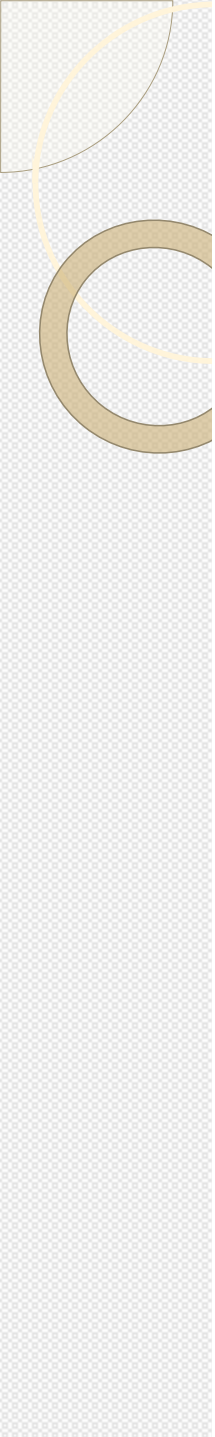
Procedure

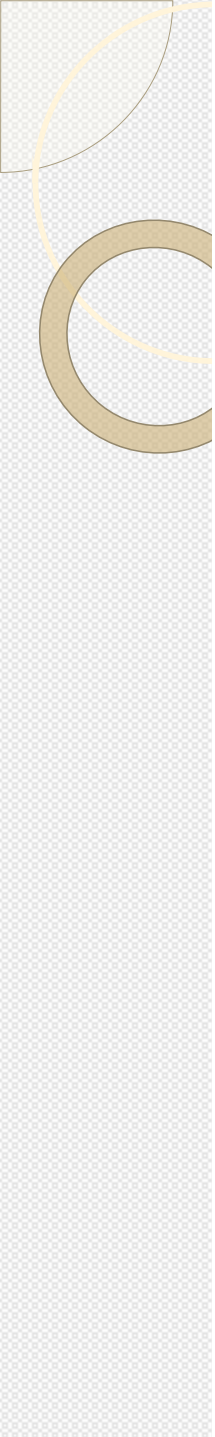
- The injected Lu-177-DKFZ-617 activity was ranged from 185 to 210 MBq with a mean of 192.6 ± 11.0 MBq
- a double headed gamma camera equipped with medium energy parallel whole collimator was used for anterior and posterior WBS at 4 24 48 and 72 hours after administration of Lu-177-DKFZ-617 obtained at a scan speed of 10 cm/min

- 
- Blood samples at 3, 10, 20, 40, 60 and 90 minutes, 2, 3, 24, 48 and 72 hours after Lu-177-DKFZ-617 infusion were obtained and 0.5 ml whole blood samples were counted in a well counter calibrated for Lu-177.
 - System calibration factor was defined by counting a known activity with different acquisition speeds taking in consideration a standardized geometry in air relative to the scintillation camera, and using similar camera acquisition settings and usually used for scan.

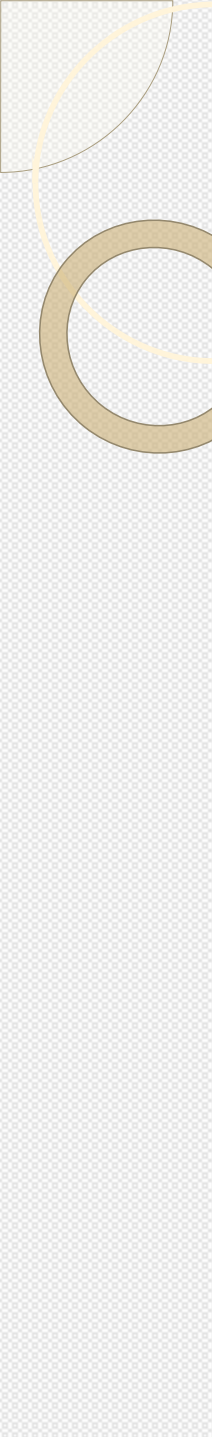
Activity Quantification

$$\mu_e = \left(\frac{1}{t}\right) \sum_{i=1}^n (\mu_i t_i - \mu_j) + \left(\frac{1}{t}\right) \sum_{i=1}^n (\mu_i - \mu_j) t_i$$



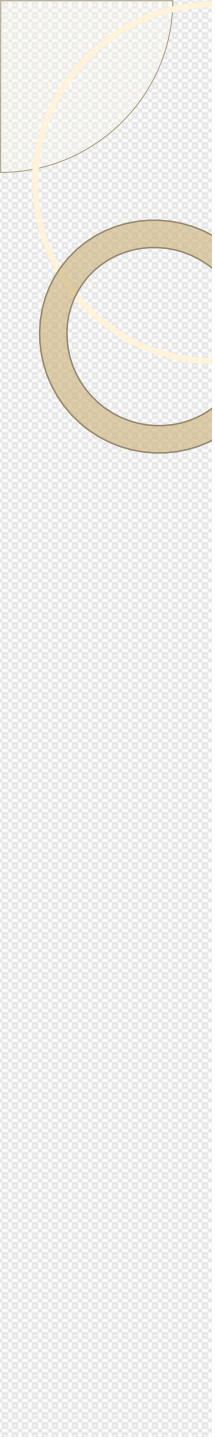


Absorbed Dose Calculation



Results

- All patients tolerated very well and we did not observe any side effect. We did not observe any change in blood pressure, heart rate or body temperature
- The radiotracer uptake decreased substantially in images obtained at 120 hours
- Half life of the distribution phase was calculated to be 17.45 ± 11.7 min and the half life of elimination phase was calculated to be 10.2 ± 5.31 hours

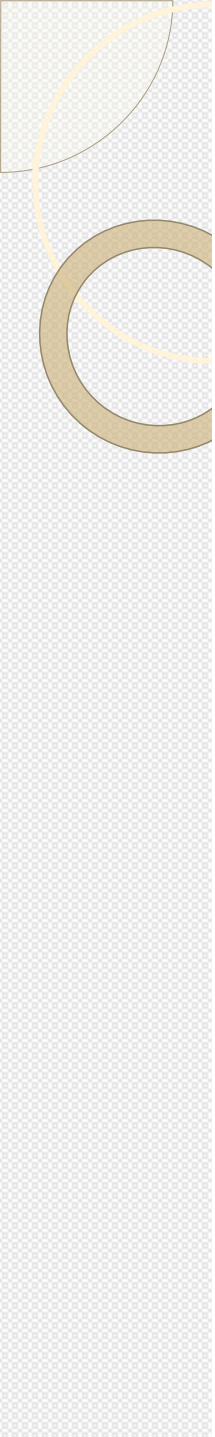
- 
- Whole body residence time showed great variation among patients and it was ranged from 24.6 hours to 62 hours with a mean value of 37.87 ± 14.61 hours.

- Bone marrow absorbed Dose mGy/mCi

Patients	Total Bone Marrow dose	Bone Marrow self dose	Percentage
1	1.13	0.199	%17
2	2.56	0.794	%31
3	1.27	0.280	%22
4	0.83	0.266	%32
5	1.70	0.440	%25
6	1.46	0.198	%13
7	0.82	0.167	%21
Mean	1.39	0.334	%23
±Sd	0.56	0.206	

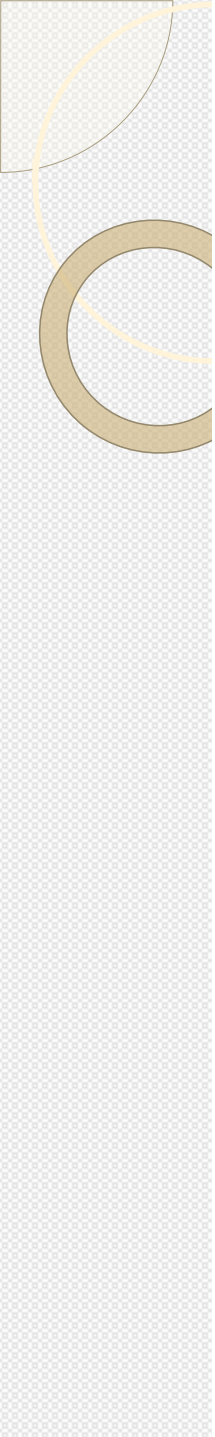
Critical Organ Absorbed Dose mGy/mCi

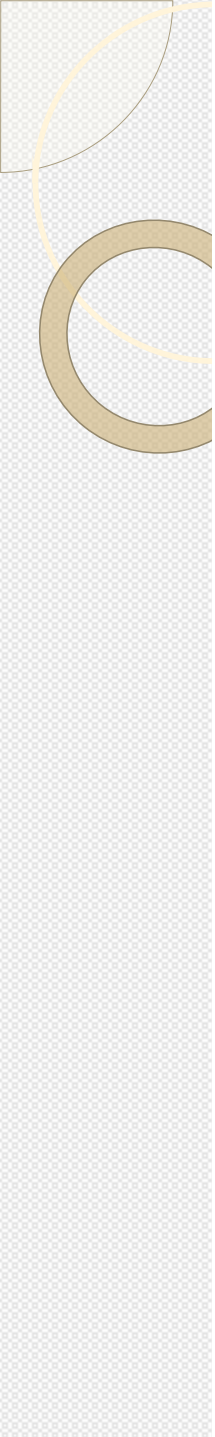
Patient	Liver	Right Kidney	Left kidney	Rt.Parotid	Lt Parotid
1	10,16	27,25	28,69	58,35	64,46
2	16,99	57,37	65,73	-----	-----
3	8,60	36,64	35,76	35,24	34,67
4	9,37	16,82	21,87	59,43	50,12
5	12,46	26,41	24,91	36,04	43,35
6	8,31	41,59	34,40	39,59	52,97
7	6,53	22,80	15,13	34,16	25,08
Mean	10.35	32.7	32.35	43.8	45.11
±SD	3.44	13.6	16.3	11.8	13.9



Discussion

- From our data the amount of radiation absorbed dose given to the bone marrow is 0.03 ± 0.01 per MBq and it seems that it is safe to administer up to a mean of 65 GBq of Lu-177-PSMA
- The calculated bone marrow radiation absorbed doses with Lu-177-DOTATE have been reported to range from 0.03 mGy to 0.07 mGy per MBq

- 
- In order to reach the dose limit to the kidneys a mean of 34 GBq of Lu-177-dota-611 can be given. This amount of activity is perfectly correlated with the radioactivity amount found for Lu-177-DOTATATE treatment which was found to be 30 GBq
 - Salivary gland damage and development of xerostomia is a frequent side effect of radiation therapy
 - maximum amount of Lu-177-DKFZ-617 that can be given to reach 30 Gy radiation absorbed dose is calculated to be 27 GBq and again it showed considerable variation among patients, ranging from 18 GBq to 37 GBq.

- 
- No scatter correction applied because of the low activity administered in order to avoid noise even it leads to overestimation to dose limiting organs
 - Prostate cancer cause severe bone metastases so depending on blood based models to estimate bone marrow absorbed dose may substantially degrade the accuracy of estimation
 - The background of overlapping tissue appears nonuniform in comparison to Lu DOTA-TATE in which more complex background subtraction approach has to be made .

Conclusion

- Lu-177-DKFZ-617 Prostate Specific Membrane Antigen (PSMA) seems to be with no hazards and promising.
- Patient specific dosimetry very recommended due to the variation in the absorbed doses among our sample
- 3D dosimetry is expected to be more innovative for better determination the overlying tissue activity and background correction.
- Bone marrow quantification through conjugate views will be helpful in bone marrow dose calculation parallel to the current blood based model.

Thank you for Attention

