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Optimization of Dose and Imaging Time for 99mTc-Zoledronic Acid for Osteoscintigraphy

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Abstract-2 : Aim: to study the optimal dose and optimal time of human skeletal imaging using tc99m-za.
Materials: 30 consecutive patients referred to the nuclear medicine department for bone scan were enrolled for the study after a valid consent.
Methods: the patients were divided into subgroups as described. Tc99m-za was prepared as per the standardized protocol. Patients were divided into 3 groups of 10 each. Group a1 was injected intravenously 5 mci of tracer, group a2 was injected 10 mci of tracer and group a3 was injected 15 mci of tracer. The patients were asked to maintain good hydration. In each group the images were acquired at 1, 2, 2.5 hour(s) after tracer injection in all the patient groups in whole body mode using lehr collimator. After completion of the study, the images were interpreted independently by two observers for the presence of adequate tracer uptake in the skeleton and also for optimal bone to background ratio. Their findings were then compared and when differences were there the decision was finalized by consensus.
Findings: the skeletal images obtained using tc99m-za were quite similar to those obtained with tc99m mdp. The optimal dose for skeletal scintigraphy using tc99m-za was 15 mci. The optimal timing post tracer injection was 2 hours.
Conclusion: the images obtained with tc99m-za are very encouraging. Their revelation of human skeleton matches with that is achieved with established agent tc-mdp. However, further studies with a large cohort of patients are warranted for clinical use of tc99m-za and establish its performance vis a vis tc99m-mdp.

I. INTRODUCTION

There are many osteoscintigraphy radiopharmaceuticals available and search for the best is always on. The Zoledronic acid is a new radiopharmaceutical for the bone scintigraphy and it belongs to a class of drugs known as bisphosphonates. This class of drugs possesses a strong affinity to bone tissue and markedly inhibits osteoclast activity 1 (Cremers et al., 2005) Bisphosphonates are basically hypercalcemic drug and used to treat bone diseases such as osteoporosis and cancer-induced bone pain and fracture. 2 (Li X[1], Naguib YW[1], Cui Z[2]).
The radio labeling of Zoledronic acid with Technetium 99m has a potential radiopharmaceutical for bone imaging because of its higher affinity to bone tissue. It can also provide efficient bone gamma imaging parameters with for bone imaging.
Radiation dose for all nuclear medicine and molecular imaging procedures should be optimized so that the patient receives the smallest possible amount of radiopharmaceutical that will provide the appropriate diagnostic information. 2, 3 http://www.snmmi.org/ClinicalPractice/DoseOptimization.aspx?ItemNumber=7317
Imaging time is also crucial factor the early imaging of patient, management of workload and providing a good quality imaging from a less radiation dose.

II. OBJECTIVE

The main objective of the study is to do optimization of dose (99mTc-ZA dose) and time for bone scintigraphy.

III. MATERIAL

A total of 50 patients, were enrolled for the study after obtaining their consent and approval from institutional ethics committee. They were divided into five groups based on dose, 10 patients in each group. D1:5mCi (185Bq), D2:10mCi (370MBq), D3: 15mCi, (555MBq), D4: 20mCi (740MBq), D5:25mCi (925MBq). The imaging time also divided in five time intervals Scanning time intervals, T1: 60min, T2: 90min, T3: 120min, T4: 150min and T5: 180min.

A. Inclusion and Exclusion criteria

The cases amongst the patients referred for the bone scintigraphy were randomly selected. No pregnant females and children below 18 years of age were included. Only those cases were selected who did not have any kind of intervention including chemotherapy, radiotherapy or surgery for their condition. Patients were advised to take plenty of fluids before coming for the study.

B. Chemical

$99mTcO^{-4}$ is procured in the form of 99Mo/99mTc Generator from Paras Isotope, Iran. Zoledronic Acid kit was a kind of gift from Sanlar Imex, Mumbai. Other chemicals of high and analytical grade were used from hospital radio pharmacy laboratory without further purification. 0.22 micron syringe filter imported from Millex Millore, Merck, Ireland. Radio Chemical Purity testing kits (Paper and ITLC) kits procured from from BRIT, Mumbai. Other equipments, instruments and consumables used form radio pharmacy laboratory.

Equipments: Gamma Counter, SPECT Gamma camera, Symbia, Siemens, Germany, for data acquisition and analysis. Other computer and software also used for the analysis of the data. The formulated kit contained a white or nearly white powder in the form of cakes or individual units, or powder. In Solution it's a colorless transparent liquid. One kit contained 1.5 mg quantity of ZA along with 0.33mg of Tin dichloride anhydrous ($SnCl_2$).

C. Administration of radiopharmaceutical

Radiopharmaceutical was administered intravenously as per the pre decided dose categories with the help of IV cannula.

II. EXPERIMENT

A. Gamma Scanning and Imaging Parameters

The study is carried out using a gamma camera by scintigraphy of the whole body in the front and rear projections 1-2 hours after administration of the drug with the obligatory prior emptying of the bladder. Interpretation of results of research carried out by two independent nuclear medicine physicians assessing the distribution of the 99mTc-ZA in the skeleton.

For examinations of the entire skeleton, anterior and posterior whole-body images of the entire axial and appendicle skeleton are standard. 4 ACR–SPR PRACTICE PARAMETER FOR THE PERFORMANCE OF SKELETAL SCINTIGRAPHY (BONE SCAN). Revised 2017 (Resolution 28)* Whole body and static Imaging was done with the help of dual head gamma camera (Symbia, Siemens). Whole body minimum: 1 million (1000K) counts and 500K counts taken for static images. Matrix: Whole-body views were obtained in a 256 × 1024 × 16 matrix. Imaging parameters were kept similar for all the patients. Data Analysis was done by two independent Nuclear Medicine physicians. The result was objective in form that target to background ratio was used as the basis of optimal image timing. The overall image quality of the studies was noted.

B. Dose and Time Optimization

For the objective of radiopharmaceutical dose optimization we have formed the five dosing categories: D1:5mCi (185Bq), D2:10mCi (370MBq), D3: 15mCi, (555MBq), D4: 20mCi (740MBq), D5:25mCi (925MBq). And for the imaging time we have made five set of imaging interval for the each dose category (10 patients) T1: 60min, T2: 90min, T3: 120min, T4: 150min and T5: 180min). Every patient scanned for five different set of time.

Bone (Target) average counts were taken from femur and Soft tissue (Background) counts were taken from thigh by drawing an ROI. Average counts were taken for each of dose category.

IV. RESULTS AND DISCUSSION

We have done analysis of the counts of the target and background for the all the five dose categories. The gamma imaging has been done over five different sittings. The average counts taken from ROI over target (femur bone) and background (thigh tissue) have been considered for all the patients.

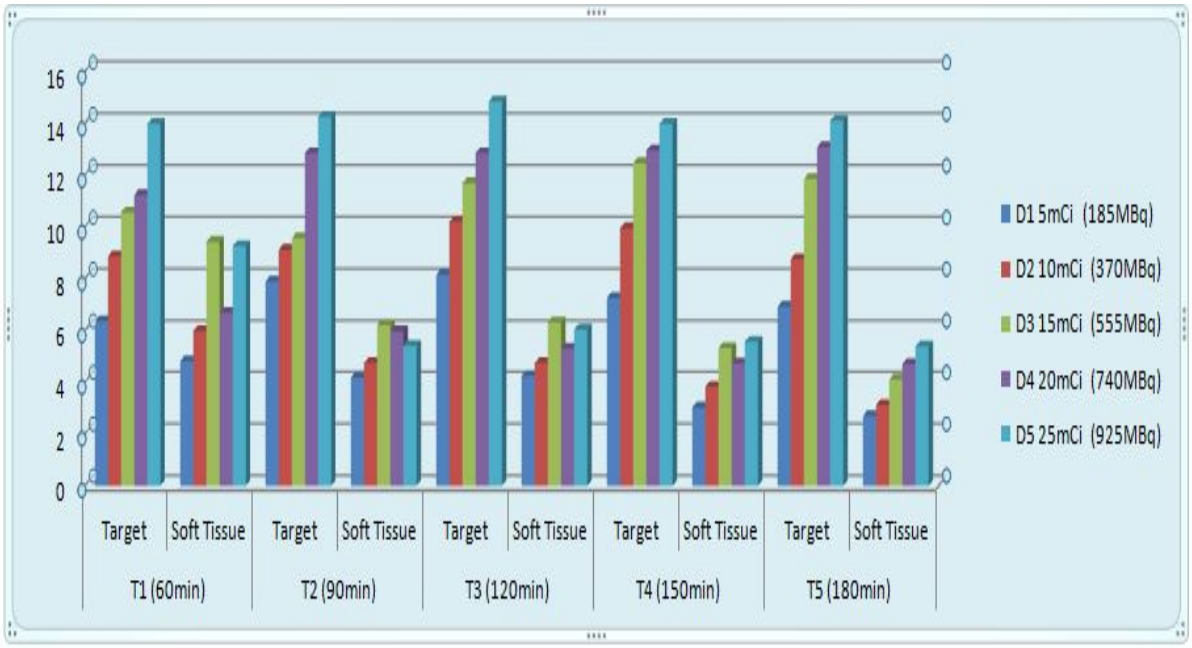
Table1. Target (Bone) and background (soft tissue) counts (average) for different dose categories and time intervals

Category	Adm. Activity	Average Counts at Different Time Interval (set of 10 patients)									
		T1 (60min)		T2 (90min)		T3 (120min)		T4 (150min)		T5 (180min)	
		Target	Soft Tissue	Target	Soft Tissue	Target	Soft Tissue	Target	Soft Tissue	Target	Soft Tissue
D1	5mCi (185MBq)	6.35	4.81	7.89	4.17	8.15	4.24	7.26	3.02	6.92	2.7
D2	10mCi (370MBq)	8.86	5.98	9.11	4.74	10.2	4.74	9.95	3.82	8.75	3.12
D3	15mCi (555MBq)	10.56	9.42	9.56	6.2	11.69	6.31	12.46	5.32	11.85	4.11
D4	20mCi (740MBq)	11.23	6.68	12.85	5.97	12.85	5.3	12.95	4.72	13.08	4.7
D5	25mCi (925MBq)	13.98	9.25	14.25	5.41	14.85	6.03	13.98	5.56	14.1	5.38

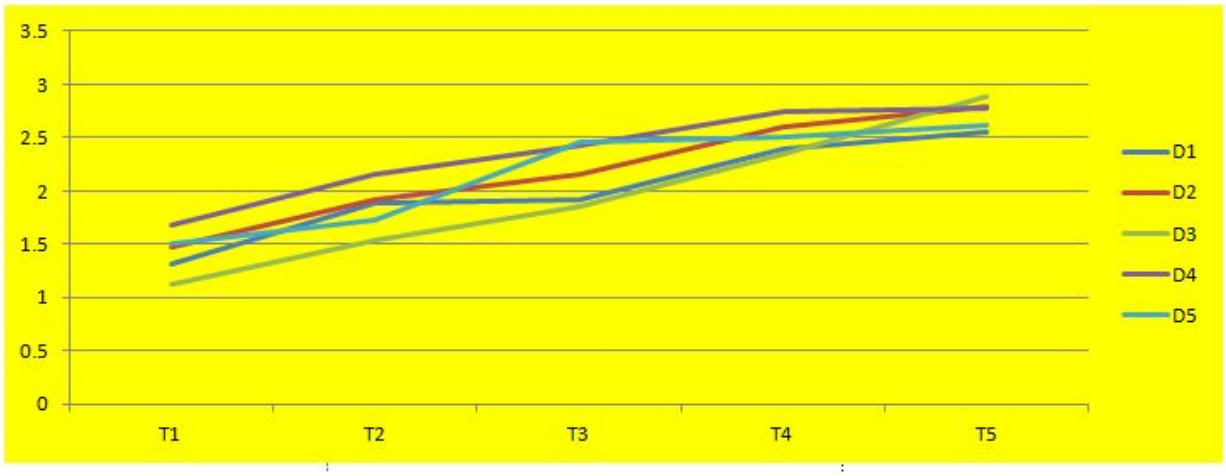
Table2. Target (Bone) and background (soft tissue) ratio for different dose categories and time intervals

Bone to Soft tissue Ration at diff time Interval for each dose set of patients					
	T1	T2	T3	T4	T5
D1	1.32	1.89	1.92	2.4	2.56
D2	1.48	1.92	2.15	2.6	2.8
D3	1.12	1.54	1.85	2.34	2.88
D4	1.68	2.15	2.42	2.74	2.78
D5	1.51	1.72	2.46	2.51	2.62

Graph1. Target (Bone) and background (soft tissue) counts (average) for different dose categories and time intervals



Graph 2: Target (Bone) and background (soft tissue) ratio for different dose categories and time intervals



Optical imaging for all five dose categories

Figure 1. Optical image for D1 Dose category

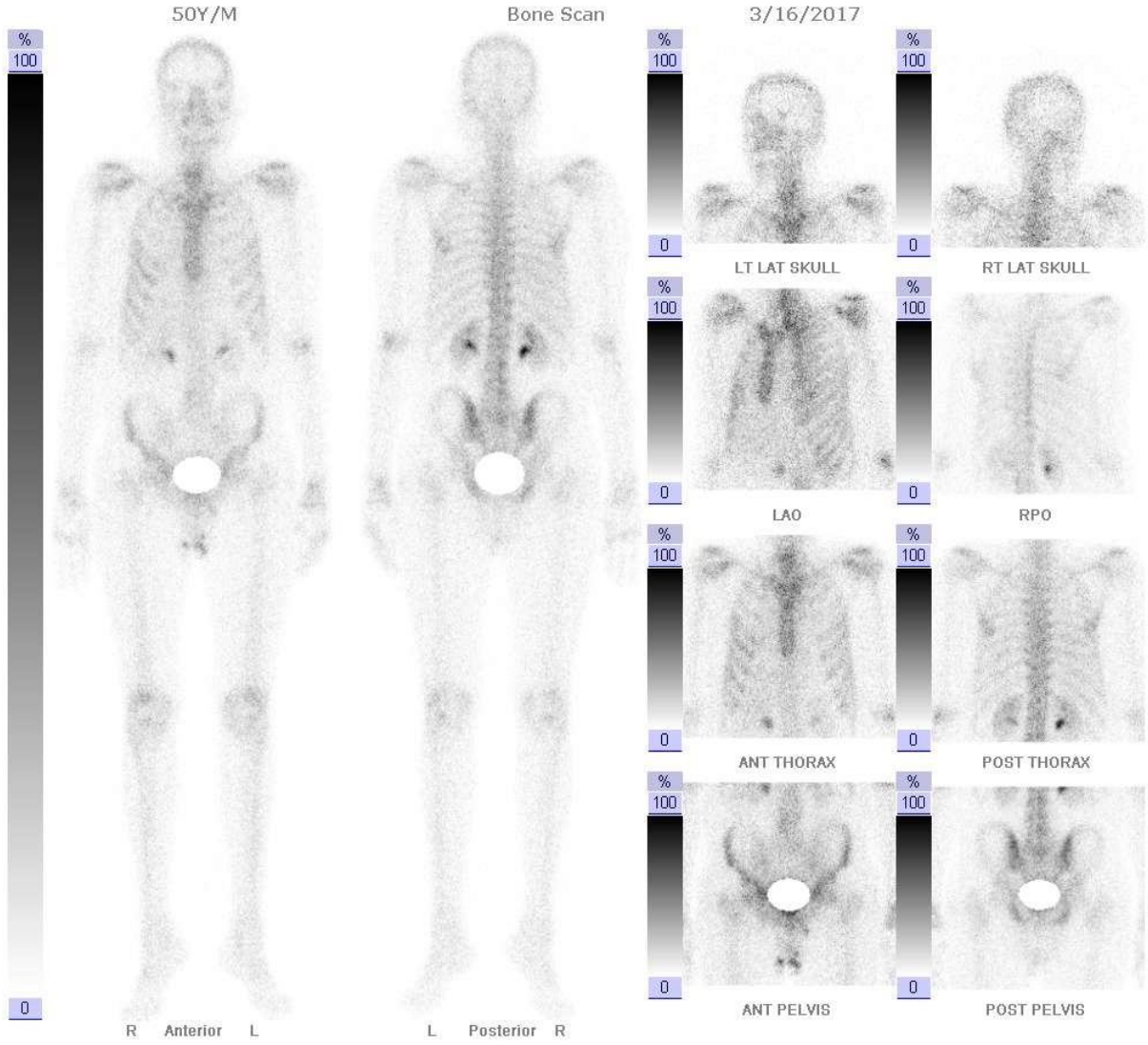


Figure 2 Optical image for D2

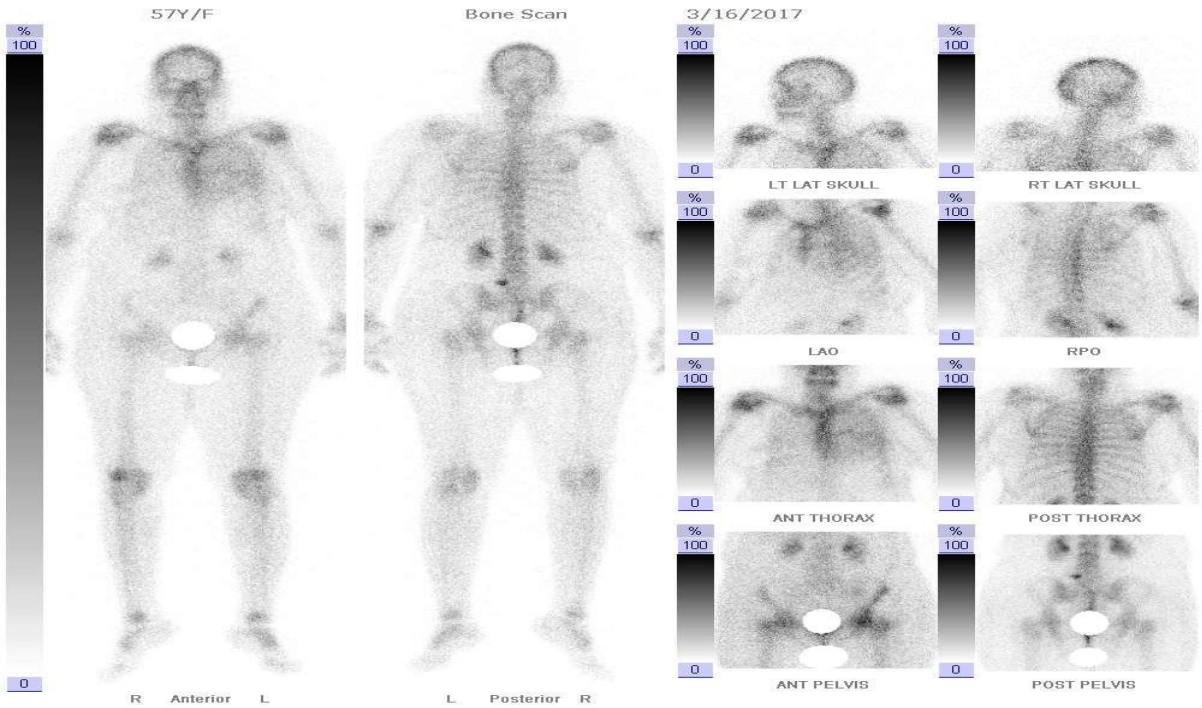


Figure 3 Optical image for D3

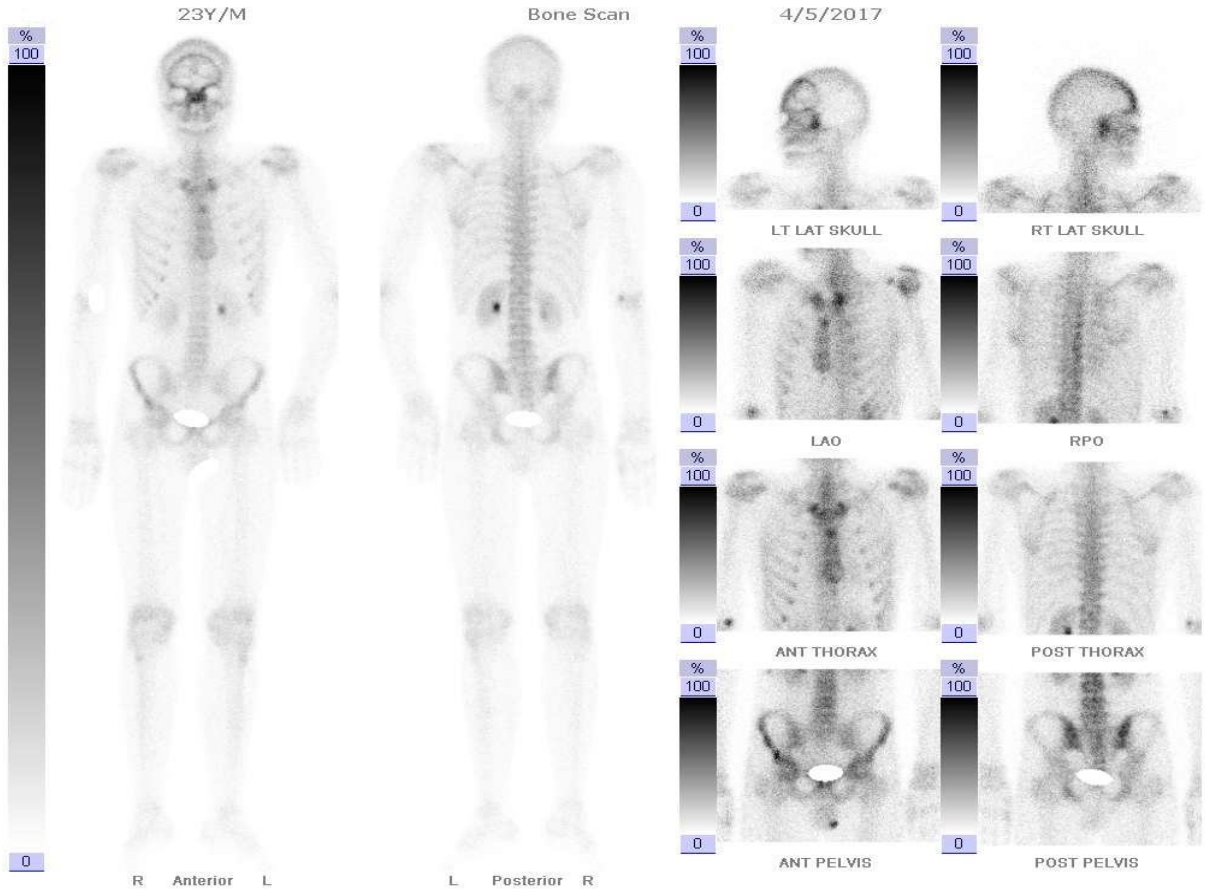


Figure 4 Optical image for D4

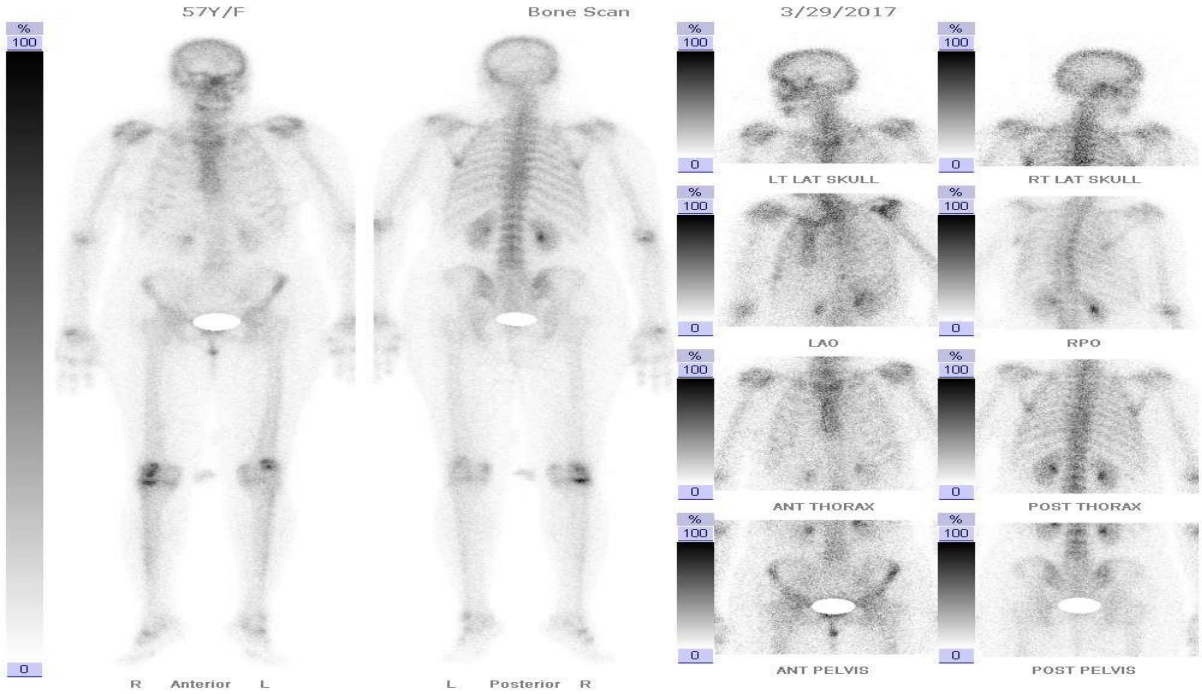
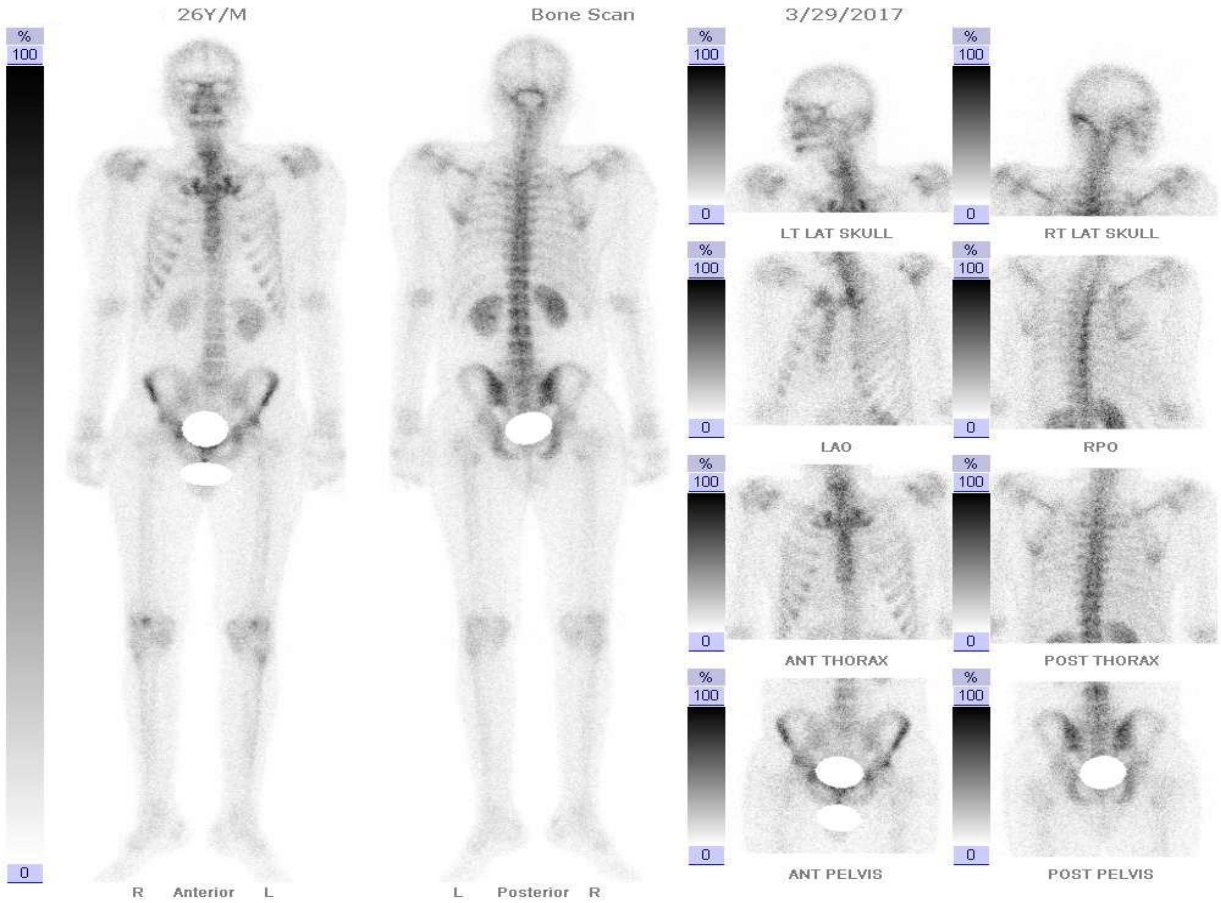


Figure 5 Optical image for D5



In the above study we can interpret that best ratio of target is background is always better for nuclear imaging. We have found the D3, 15mCi and D4: 20mCi doses are better and reasonable good for imaging of 99mTc-ZA and gives satisfactory results and good imaging data.

The international commission of radiation protection (ICRP) and the International atomic energy agency (IAEA) recommend the patient dose must be kept as low as reasonably achievable and from radiation protection and ALARA principle we have to use the minimum dose of radiopharmaceutical to get the desired results. **5**, **IAEA, face sheet, radiation in every life, 2016.** Optimization of time is again curial factor because that not only save the patient time also help in the management of departmental workload.

Radio pharmaceutical dosages for specific indications are optimized based on thorough studies performed on animals and through clinical trials on human subjects prior to approval for clinical applications. 6

Book Author, Xiaowei Zhu, Springer, Dosages of Radiopharmaceutical and Internal Dosimetry

V. CONCLUSION

From the above study we have observed that the optimal dose for bone scintigraphy for 99mTc-ZA is 15mCi to 20mCi (D3 and D4 dose categories) and optimal time for imaging is 120 min (T4 time category) for reasonable good quality imaging.

However this study was limited to 10 patients (each category) data so further more number of patients data can be evaluated for deriving a standard dose and standard imaging time for 99mTc-ZA bone scintigraphy.

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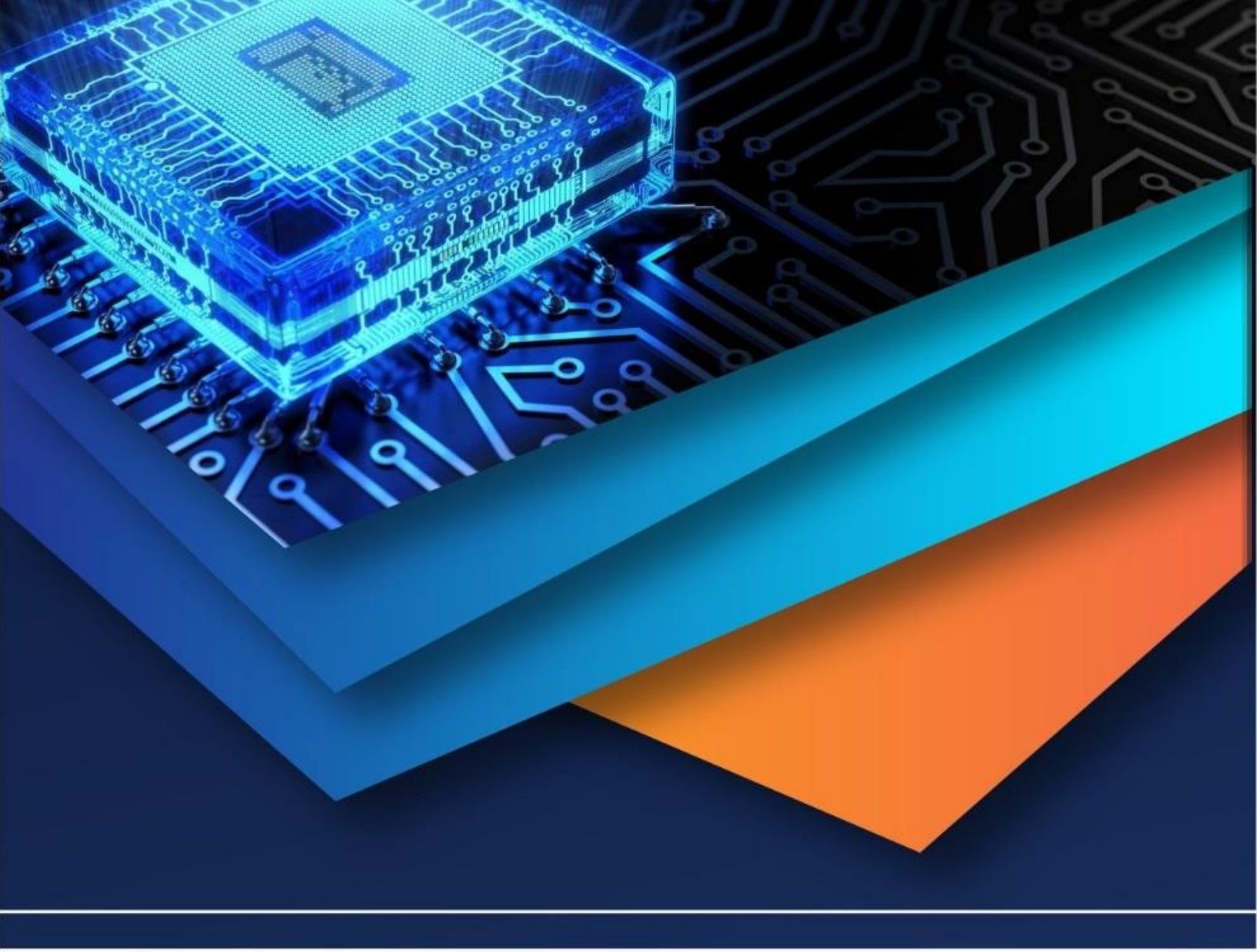
[5] IAEA, facesheet, radiation in every life 2016

[6] Book Author, Xiaowei Zhu Spinger , Dosages of Radiopharmaceutical and Internal Dosimetry



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