SHORT COMMUNICATION

Evaluation of Tl-201 SPECT imaging findings in prostate cancer

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Summary
Objectives: To compare with histopathologi-cal findings the findings of prostate cancer imaging by SPECT method using Tl-201 as a tumor seeking agent.
Methods: The study comprised 59 patients (age range 51-79 years, mean age 65.3 ± 6.8 years) who were planned to have transrectal ultrasonography (TRUS)-guided biopsies due to suspicion of prostate cancer between April 2011 and September 2011. Early planar, late planar and SPECT images were obtained for all patients. Scintigraphic evalua-tion was made in relation to uptake presence and patterns in the visual assessment and to Tumor/Background (T/Bg) ratios for both planar and SPECT images in the quantitative assessment. Histopathological findings were compatible with benign etiology in 36 (61%) patients and malign etiology in 23 (39%) patients. Additionally, comparisons were made to evaluate the relationships between uptake patterns, total PSA values and Gleason scores.
Results: A statistically significant difference was found between the benign and malignant groups in terms of uptake in planar and SPECT images and T/Bg ratios and PSA val-ues. No statistically significant difference was found between uptake patterns of planar and SPECT images and Gleason scores in the malignant group.
Conclusions: SPECT images were superior to planar images in the comparative assessment. Tl-201 SPECT imaging can provide an additional contribution to clinical practice in the diagnosis of prostate cancer and it can be used in selected patients.

KEY WORDS: *Prostate cancer; Scintigraphy; Thallium chloride (Tl-201); SPECT.*

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INTRODUCTION

Prostate cancer is one of the leading causes of cancer related deaths in men. Risk factors include age, race, socioeconomic status, family history, genetic factors, obesity and infections (1-3). Adenocarcinomas are the most common tumors of the prostate gland with more than 90% being of epithelial origin. Diagnostic methods used for the early diagnosis of prostate cancer are digital rectal examination (DRE), serum prostate-specific anti-gen (PSA) levels and transrectal ultrasonography (TRUS)-guided biopsy. In the determination of prostate cancer risk, a combination of serum PSA and DRE is the most useful primary option (4). PSA value is not specif-ic for prostate cancer (5) and there is no definite cut-off value of PSA to detect prostate cancer (6). TRUS is not recommended as the primary diagnostic modality due to its high cost price and low predictive value (7). However, the histopathological grading of prostate tissues obtained by TRUS-guided biopsy is the gold standard method for diagnosing prostate cancer.
Nuclear medicine had an important role in the diagnosis, treatment planning, and in the evaluation of treatment effectiveness in cancer patients. There are many options such as bone scintigraphy, tumor imaging studies with Tc-99m methoxy isobutyl isonitrile, thallium chloride (Tl-201), gallium 67 (Ga-67) citrate etc. and Positron emission tomography (PET) with F-18-fluorodeoxyglu-cose and other specific radiopharmaceuticals that have an important place in oncological imaging (8).
The aim of this study was to show routine clinical use and effectiveness of Tl-201 Single Photon Emission Tomography (SPECT) in the detection of prostate cancer.

MATERIALS AND METHODS

Patient group
Between April 2011 and September 2011, 59 patients with a mean age of 65.3 ± 6.8 years (range 51-79 years,) who were planned for a TRUS-guided biopsy according to the results of TRUS and serum PSA levels or who were planned for a TRUS-guided biopsy, were included in this study. Tl-201 planar and SPECT imaging were per-formed on the patients prior to the prostate biopsies. Informed consent was obtained from all patients prior to scintigraphic imaging.

Scintigraphic studies
Twenty minutes after intravenous administration of 2 mCi (74 MBq) Tl-201, the scintigraphic images were obtained from the pelvic region with a double-headed gamma camera in the supine position. Early static imag-ing was performed for five minutes Abduction of the lower limbs was carried out to obtain better anatomic localization. Following the early static images, SPECT imaging was carried out . One hour after the injection,

scintigraphic examinations were terminated by taking late static images for five minutes.

Evaluation of scintigraphic images

Images were evaluated qualitatively and quantitatively with a joint decision of two blinded Nuclear Medicine specialists with at least 5 years experience in the field. Visual scintigraphic assessment was made to assess the presence or absence of tumor uptake in the early and late planar SPECT images. In addition, the group with tumor uptake was divided into subgroups of mild, moderate and significant levels of uptake according to the radioactivity uptake patterns. For quantitative evaluation, tumor/background (T/Bg) ratios were calculated by drawing a similar region of interest (ROI).

Histopathological evaluation

The pathological results of the TRUS-guided needle biopsy were evaluated in a separate session. The patients who were reported as benign etiology, atypical small acinar proliferation (ASAP), chronic prostatitis and lesion with low malignant potential were classified as the benign group. Otherwise the patients who were reported as adenocarcinoma were classified as the malignant group. Whether there was uptake or not and the type of uptake patterns were analyzed according to the results of the pathological examination.

The relationships between them were evaluated by comparing the PSA values and Gleason scores of the malignant group and the PSA values of the benign group with the presence of uptake and its uptake pattern.

Gleason scores were grouped as Gleason 1 (the most common pattern), Gleason 2 (the second most common pattern) and Gleason Total (total score). The relationships among the Gleason scores and early and late planar and SPECT images were evaluated separately. The relationship between the uptake patterns and T/Bg ratios was examined for both the benign and malignant groups.

Statistical analysis

Data analysis was performed using SPSS software for Windows 11.5 package program. Student's t-test and Mann-Whitney U test were respectively used to evaluate the significance of the difference between the groups for averages and median values. Categorical variables were evaluated with Pearson's chi-square test.

The statistical significance of T/Bg ratios for the images to distinguish between the malignant and benign groups was assessed by calculating the area under the ROC curves. A level of $p < 0.05$ was considered as a statistical significance for the results.

RESULTS

Following the scintigraphic imaging with Tl-201 of 59 male patients, the biopsy specimens were evaluated histopathologically. The results were reported as benign lesions in 36 (61%) and malignant lesions in 23 (39%) patients. In the malignant group, all the patients' biopsy results were adenocarcinoma of the prostate gland. In the benign group, the biopsy results were reported as benign pathological features in 27 patients, ASAP in 5 patients, chronic prostatitis in 3 patients, lesion with low potential for malignancy in only 1 patient. There was no statistically significant difference (p = 0.304) between the benign and malignant groups of the patients respect to the mean ages (benign: 64.6 ± 6.9 years; malignant: 66.4 ± 6.6 years). Average PSA values were 7.03 ± 3.89 ng/ml (min.-max.; 2.58- 24.61) in the benign group and 29.5

Figure 1. *A pathological Tl-201 uptake in the prostatic region is not shown on the early (P: Prostatic region; B: Background) (A), late (B) planar images. It is noteworthy that the increase in activity in the bladder. Transverse SPECT (C) images show a lack of a pathological Tl-201 uptake in the prostatic region Coronal SPECT (D) images show a pathological uptake in the prostatic region.*
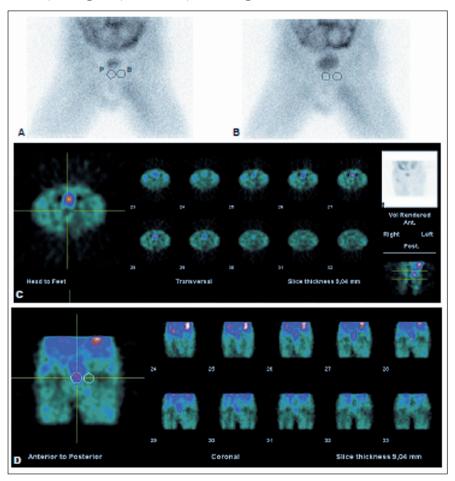
Table 1.

Diagnostic performance indicators obtained by ROC analysis for T/Bg ratios.

Indicators	Definitions	Early T/Bg	Late T/Bg	SPECT T/Bg
AUC		0,659	0,684	0,912
95% CI		0,514-0,805	0,548-0,819	0,831-0,993
Cut Point		1.104	0.997	1.239
Sensitivity	TP/(TP+FN)	13/23 (56.5%)	23/23 (100.0%)	22/23 (95.7%)
Specificity	TN/(TN+FP)	27/36 (75.0%)	13/36 (36.1%)	28/36 (77.8%)
PPV	TP/(TP+FP)	13/22 (59.1%)	23/46 (50.0%)	22/30 (73.3)%
NPV	TN/(FN+TN)	27/37 (73.0%)	13/13 (100.0%)	28/29 (96.6%)
Accuracy	(TP+TN)/(N)	40/59 (67.8%)	46/59 (78.0%)	50/59 (84.7%)
p value	(Chi-Square Test)	0.015	< 0,001	< 0.001

AUC: Area Under Curve, CI: Confidence Interval, TP: True Positive, FN: False Negative, TN: True Negative, FP: False Pozitive, PPV: Pozitive Predicted Value, NPV: Negative Predicted Value.

± 71.57 ng/ml (min.-max.; 3.70-347.23) in the malignant group. PSA values showed a statistically significant difference (p < 0.05) between two groups.

Early and late static planar and SPECT images were visually grouped according to the presence or absence of Tl-201 uptake (Figure 1).

Ten of 36 (27.8%) patients with a benign lesion and 16 of 23 (69.6%) patients with malignant lesion had Tl-201 uptake in the early planar images and 10 (27.8%) patients with a benign lesion and 17 (73.9%) patients with malignant lesion had Tl-201 uptake in the late planar images.

There was a statistically significant difference for the presence of early and late Tl-201 uptake between the malignant and benign lesion groups (p = 0.002 and p = 0.001, respectively).

SPECT images were evaluated according to the presence of Tl-201 up take and Tl-201 uptake was observed in 20 (55.6%) patients in the benign group and in 20 patients (87%) in the malignant group.

Table 2.

Distribution according to the Tl-201 uptake patterns for Gleason 1, Gleason 2 and Gleason total in the early, late and SPECT images.

Variables	Patern 0-1	Patern 2-3	p-value
Early			
Gleason 1	3 (3-4)	3 (3-4)	0.376 a
Gleason 2	3 (2-5)	3 (2-4)	0.720 a
Gleason Total	6 (5-8)	7 (5-8)	0.769 a
Late			
Gleason 1	3 (3-4)	3 (3-4)	0.506 a
Gleason 2	3 (2-5)	3 (2-4)	0.636 a
Gleason Total	6 (5-8)	6 (5-8)	0.975 a
SPECT			
Gleason 1	3 (3-4)	3 (3-4)	0.975 a
Gleason 2	3 (3-4)	3 (2-5)	1.000 a
Gleason Total	6 (6-8)	6 (5-8)	0.925 a

a: Mann Whitney U test.

There was a statistically significant difference (p = 0.012) between the malignant and benign groups

The incidence of Tl-201 uptake was also higher for all images in the malignant group than in the benign group. T/Bg ratios were found to be higher in the malignant group than in the benign group for the three types of image.

There were statistically significant differences for T/Bg ratios among all groups.

This difference was more significant for SPECT images (p < 0.001).

The diagnostic performance of T/Bg ratios obtained from the early planar, late planar and SPECT images was demonstrated by ROC analysis to discriminate between malignant and benign cases. According to these results, the areas under the curve for T/Bg ratios in the early planar, late planar and SPECT images were respectively determined to be 0.659 ± 0.074, 0.684 ± 0.018 and 0.912 ± 0.041. The differences were statistically significant (p < 0.05). Sensitivity, specificity, accuracy, positive and negative predictive values were calculated for the three types of image.

The results are shown in Table 1. Statistically significant differences were determined (p < 0.001) for the diagnostic performance of these imaging types.

The correlations between the uptake patterns and T/Bg ratios of the early, late planar and SPECT images were examined. There was a statistically significant difference (p < 0.001) and a direct correlation between them. SPECT image for this correlation was stronger than the other types of imaging.

The presence of Tl-201 uptake and uptake patterns of the images in the malignant group of patients were evaluated by a comparison with Gleason scores.

The most common Gleason pattern was considered to be Gleason 1. Median (minimum ; maximum) values were calculated as 3 (min: 3; max: 4) in Gleason 1, 3 (min: 2; max: 5) in Gleason 2 and 6 (min: 5; max: 8) in Gleason total. No statistically significant difference was found between Gleason score groups and the presence of Tl-201 uptake on the images.

Likewise, there was no statistically significant correlation between the uptake patterns and Gleason score groups (Table 2).

Conclusions

In this study, statistically significant differences were obtained in terms of the presence of Tl-201 uptake, uptake patterns and T/Bg ratios between benign lesions and malignant lesions. When planar images and SPECT images were compared, the SPECT images were found to be more valuable than the planar images.

Therefore Tl-201 SPECT imaging may contribute to the differentiation of benign and malignant lesions in patients suspected for prostate cancer.

Discussion and full list of References are posted on the website www.aiua.it

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REFERENCES

1. Jemal A, Bray F, Center MM, et al. Global cancer statistics. CA Cancer J Clin. 2011; 61:69-90.

2. Albano JD, Ward E, Jemal A, et al. Cancer mortality in the United States by education level and race. J Natl Cancer Inst. 2007; 99:1384-94.

3. Kinsey T, Jemal A, Liff J, et al. Secular trends in mortality from common cancers in the United States by educational attainment, 1993-2001. J Natl Cancer Inst. 2008; 100:1003-12.

4. Catalona WJ, Hudson MA, Scardino PT, et al. Selection of optimal prostate specific antigen cut offs for early detection of prostate cancer: receiver operating characteristic curves. J Urol. 1994; 152:2037-42.

5. Gretzer MB, Partin AW. Prostat Cancer Tumor Markers, In: Walsh PC, Retik AB, Vaughan EDJ et al. Campbell's Urology, 9th Edition, Saunders, Philadelphia 2007, pp.3042-54.

6. Carter HB. A PSA threshold of 4.0 ng/ml for early detection of prostate cancer: the only rational approach for men 50 years old and older. Urology. 2000; 55:796-9

7. Flanigan RC, Catalona WJ, Richie JP, et al. Accuracy of digital rectal examination and transrectal ultrasonography in localizing prostate cancer. J Urol. 1994; 152:1506-9.

8. Eary JF. Nuclear Medicine in cancer diagnosis. Lancet. 1999; 354:853-7

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