

**OctreoSCAN IMAGING IN SOMATOSTATIN
RECEPTOR-POSITIVE CELL TUMOUR**

Donka Vassileva, Sonia Sergieva*

(Submitted by Corresponding Member M. Vlaskovska on July 12, 2012)

Abstract

Various tumours contain high numbers of somatostatin receptors, which enable the use of somatostatin receptor scintigraphy (SRS) for visualization of these tumours. The purpose of this study was to assess the value of SRS, serum β -2-microglobulin and the correlation between them for diagnosis and staging of patients with malignant lymphomas.

Forty-five patients with malignant lymphomas were investigated (20 with non-Hodgkin's lymphomas and 25 with Hodgkin's Disease). Planar and SPECT images were performed 24 and 48 h after i.v. injection of 110-185 MBq ^{111}In labelled pentetreotide (OctreoSCAN) on the rotating gamma camera (Diacam, Siemens). SRS results were compared with the data of conventional methods (clinical examination, X-ray, CT, bone marrow biopsy). β -2-microglobulin levels were measured by radioimmunoassay using the Immunotech International Microtest.

The SRS was true positive in 36 patients with malignant lymphomas. Ninety-two lesions were identified, 69 of them with nodal localization – neck, hilar, mediastinal, axillar and inguinal. 23 of all were with extranodal localization in the region of the lung, bones and stomach. Seven previously unknown

localizations were visualized in 5 patients. Additional CT and ultrasound examinations confirmed the presence of tumour tissue. The clinical staging of all these patients was changed. A significant correlation was found in patients with advanced disease with true positive SRS and a high level of serum β -2-microglobulin. In 2 patients, false positive results on SRS were found. True negative scans were obtained in 7 patients. These results indicate that malignant lymphomas express somatostatin receptors in sufficient number and density which allow tumour visualization with ^{111}In labelled Pentetreotide.

Positive SRS shows a good correlation with the data of serum β -2-microglobulin at different stages of the disease. In conclusion, SRS provides a sensitive, non-invasive diagnostic modality to localize tumour tissue of malignant lymphomas.

Key words: lymphoma, diagnosis and staging, somatostatin receptor scintigraphy, serum β -2-microglobulin

Introduction. Various tumours contain a high number of somatostatin receptors, which enable the use of somatostatin receptor scintigraphy (SRS) for visualization of these tumours [$^{1-3}$]. In vitro studies have shown that somatostatin receptors are presented in human malignant lymphoma [4]. Exact diagnosis and staging in patients with lymphomas are important for adequate treatment and good prognosis of the disease.

β -2-microglobulin ($\beta_2\text{M}$) levels have recently been used to detect tumour regression and progression in malignant lymphomas. Somatostatin receptor scintigraphy has been used in nuclear oncology, but its role in detecting lymphomas and correlation with serum $\beta_2\text{M}$ has not been widely investigated. The purpose of this study was to assess the value of somatostatin receptor scintigraphy, $\beta_2\text{M}$ and the correlation between them in patients with malignant lymphomas.

Materials and methods. Forty-five patients (23 males, 22 females) with malignant lymphomas were investigated: 20 with non-Hodgkin's lymphomas (NHL) and 25 with Hodgkin's Disease (HD). The patients' ages ranged from 21 to 69 years.

SRS was performed 24 and 48 h after i.v. injection of 110–185 MBq ^{111}In labelled pentetreotide (OctreoSCAN). Planar and SPECT images were obtained with a single-head rotating gamma camera (Diacam, Siemens) equipped with high energy all-purpose collimator. The pulse height analyser windows were centred over both ^{111}In photon peaks (172 and 246 KeV) with a window width of 15%. Anterior and posterior planar images were carried out with a matrix of 64×64 pixels, 300 000 preset counts or max 20 min at 24 h and 200 000 counts or max 20 min at 48 h after injection in the region of the head, the chest and the abdomen. SPECT image acquisition parameters were 60 projections, 64×64 word matrix, 45 s per projection.

When tumour tracer uptake was presented, a tumour uptake index (TUI) was calculated using two regions of interest (ROIs) – one over the tumour and the second over the contralateral side. The TUI was determined as the ratio of the tumour activity to the background activity.

SRS results were compared with the data of conventional methods (clinical examination, X-ray, CT, bone marrow biopsy). β_2M levels were measured by radioimmunoassay using the Immunotech International Microtest.

Results and discussion. In normal individuals, a physiological accumulation of radioactivity may be seen at 24 h after intravenous administration of ^{111}In labelled pentetretotide in the pituitary and thyroid gland, the liver, spleen, kidneys, the urinary bladder and occasionally in the gall-bladder [1, 5]. The presence of intestinal radioactivity, mainly in the colon at 24 h, is due to some hepatobiliary clearance of the radioligand. Physiological uptake may be reduced following the use of laxatives. Additional radioactivity in organ-like configuration was regarded as indicative of the presence of lesions caused by somatostatin-expressing pathological tissue.

The SRS was true positive in 36 patients with malignant lymphomas (21 patients with HD and 15 patients with NHL). In the patients with positive scans, the results were compared with the data of conventional methods. In all of the cases, SRS fails to demonstrate active sites of the disease. The density of somatostatin receptors on these lymphomas was so high that in vivo visualization of these receptors with the ^{111}In labelled somatostatin analogue was possible.

The scintigraphic results of our patients with lymphomas are summarized on Table 1.

T a b l e 1
Results of ^{111}In -pentetretotide imaging

Number of patients: 45	Lesion location
True positive – 36 (T/B ratio 1.5-2.9)	Total – 92: ▷ Nodal – 69 ▷ Extra nodal – 23
True negative – 7	–
False positive – 2	▷ Nasal – 1 ▷ Breast – 1
False negative – 0	–

Fig. 1. SRS with ^{111}In in pentetreotide in a patient with NHL demonstrated positive right supraclavicular lymph nodes and tracer uptake in the mediastinal lymph nodes →

Fig. 2. A. SRS with ^{111}In in pentetreotide in a patient with HD demonstrated increased uptake in the mediastinal and right palpable supraclavicular lymph nodes →

Ninety-two lesions were identified, 69 of them with nodal localization in different regions: cervical, hilary, mediastinal, axillary and inguinally lymph nodes (Fig. 1, Fig. 2A, Fig. 3). Twenty-three of all were with extranodal localization in the region of the lung, bones and stomach.

When tumoral tracer uptake was presented, ROIs technique was used to calculate the target/background (T/B) ratio. Tumour uptake index ranged from 1.5 to 2.9 in the studied patients with positive SRS.

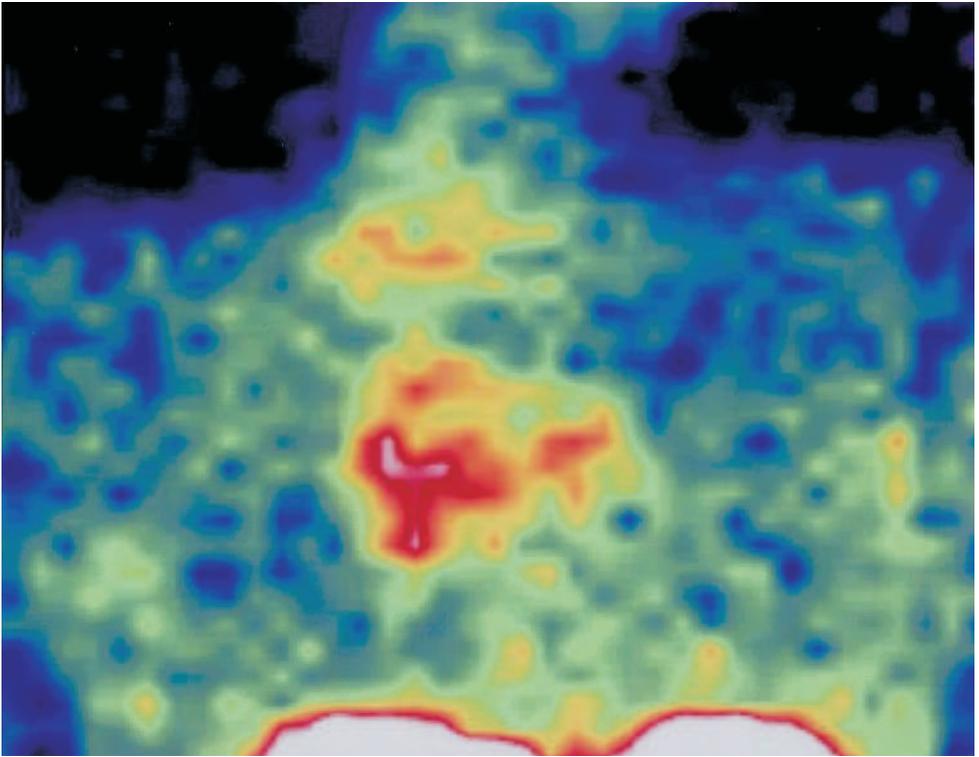
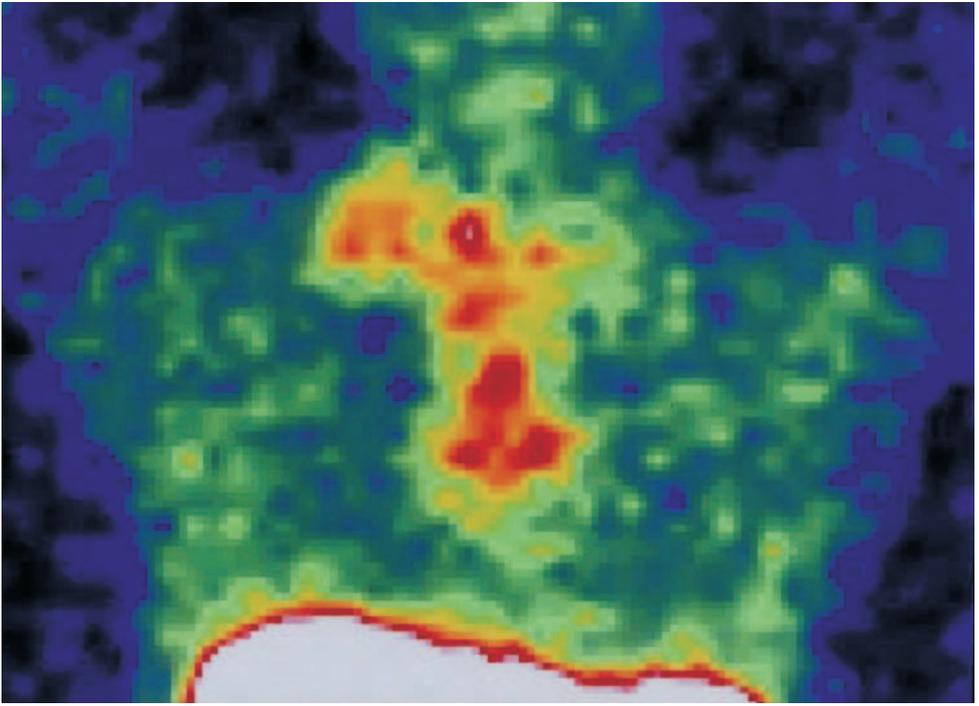
Seven previously unknown lesions were visualized in 5 patients (Fig. 2B). Most of the new localizations were above the diaphragm. Additional CT and ultrasound examinations confirmed the presence of tumour tissue. The clinical staging of all these patients were changed.

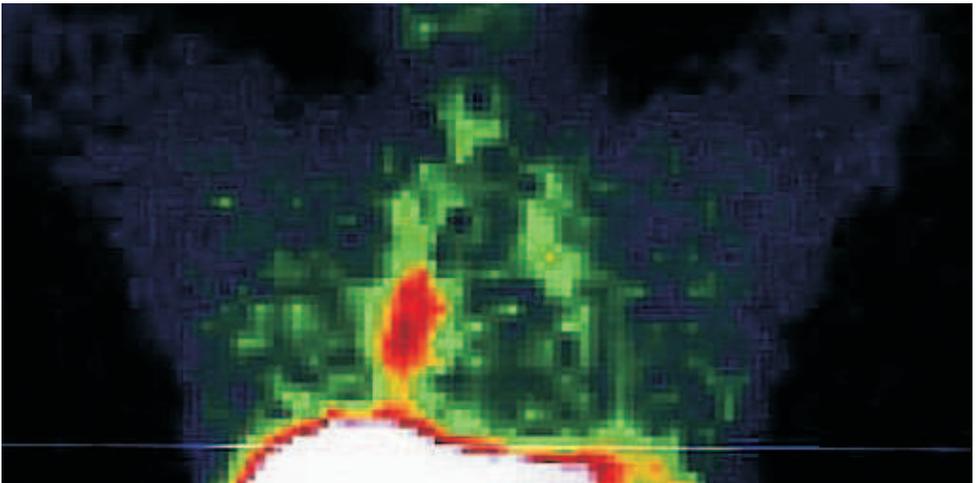
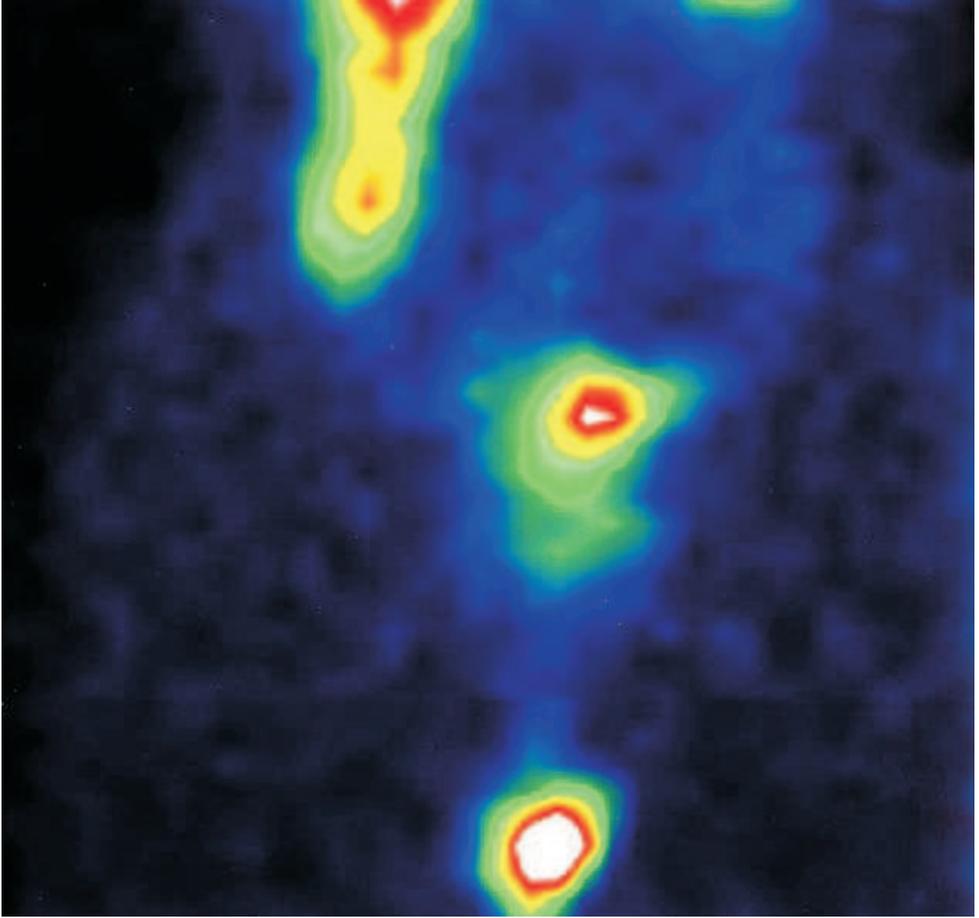
A significant correlation was found in patients with true positive SRS and a high level of $\beta_2\text{M}$. Increased values of $\beta_2\text{M}$ were found in 1 patient with true negative SRS. The clinical appearance of the disease was demonstrated in this patient two months later.

In 2 patients with normal rate of $\beta_2\text{M}$, false positive results after carrying out SRS were found. In the first patient, accumulation of radioactivity was observed in the nasal region. In the second patient, increased tracer uptake was detected in the area of the left breast. The mammography and ultrasound of the breast in this woman were normal. Breast inflammation was proved.

True negative scans were obtained in 7 patients. The diagnostic value of somatostatin receptor scintigraphy was as follows: sensitivity – 100%, specificity – 77% and accuracy – 98%.

The lesion-related sensitivity of SRS in this study is higher than that reported by other groups [4, 6, 7]. The differences in sensitivity rates may also be explained by differences in the present counting time and the specifications of the gamma camera used. The number and selection of patients may explain part of this difference in sensitivity. Furthermore, differences in imaging protocol and dosage of ^{111}In labelled pentetreotide may also play a role. Therefore, it is the opinion of some authors that counting time should be long enough and applied doses of the radionuclide should be sufficiently high [4]. Such functional imaging can complement computed tomography or magnetic resonance imaging and other scintigraphic techniques to localize these tumours before medical and radiotherapeutic approaches are considered and to follow up patients after treatment [8–10].





← Fig. 2. *B*. Focal pathological hot spot was visualized in the central abdominal region previously unknown

← Fig. 3. SRS with ^{111}In pentetreotide in a patient with HD demonstrated high uptake in lymph nodes of the right hilar region

Conclusion. These results indicate that NHL and HD express somatostatin receptors in sufficient number and density which allow exact tumour visualization and correct staging with ^{111}In labelled pentetreotide. SRS provides a sensitive, non-invasive diagnostic modality to localize tumour tissue of NHL and HD.

Positive SRS data show good correlation with levels of serum $\beta_2\text{M}$ at different stages of the diseases, which is very important for the diagnosis and follow-up of patients. As compared with conventional staging methods, SRS offers a number of distinct advantages. Because the whole body is imaged, localizations in areas not under clinical suspicion can be evaluated and therefore the full extent of the disease more accurately documented.

REFERENCES

- [1] BOBARDIERI E., V. AMBROSINI, C. AKTOLUN, R. BAUM, A. DELALOYE. *Eur. J. Nucl. Med. Mol. Imaging*, **37**, 2010, No 7, 1441–1448.
- [2] AGOOL A., R. SLART, R. DIERCKX, P. KLUIN, L. VISSER et al. *Eur. J. Nucl. Med. Mol. Imaging*, **37**, 2010, No 1, 124–130.
- [3] KWEKKEBOOM D., E. KRENNING, M. JONG. *Journal of Nucl. Med.*, **41**, 2000, No 10, 1704–1713.
- [4] LUGTENBURG P., B. LOWENBERG, R. VALKEMA, H. OEI, S. LAMBERTS. *Journal of Nucl. Med.*, **42**, 2001, No 2, 222–229.
- [5] BREEMAN W., M. JONG, D. KWEKKEBOOM, R. VALKEMA, W. BAKKER. *Eur. J. Nucl. Med. Mol. Imaging*, **28**, 2001, No 9, 1421–1429.
- [6] CHOLEWINSKI W., J. KOWALCZUK, B. STEFANIAK, J. STEFANIAK, E. FRASUNEK et al. *Eur. J. Nucl. Med. Mol. Imaging*, **31**, 2004, No 6, 820–824.
- [7] LI S., A. KURTARAN, M. LI, T. WEIDINGER, O. KIENAST et al. *Eur. J. Nucl. Med. Mol. Imaging*, **30**, 2003, No 8, 1087–1095.
- [8] KOSTAGLU L. *Eur. J. Nucl. Med. Mol. Imaging*, **35**, 2008, No 8, 1413–1420.
- [9] ILIAS I., B. SHULKIN, K. PACAK. *Trends in Endocrinology and Metabolism*, **16**, 2005, No 3, 66–72.

[¹⁰] JUWEID M. E., S. STROOBANTS, O. S. HOEKSTRA et al. *J. Clin. Oncol.*, **25**, 2007, No 5, 571–578.

*Department of Nuclear Medicine
National Hospital of Active
Treatment of Haematological Disease
6, Plovdivsko pole
1756 Sofia, Bulgaria
e-mail: vassileva@excite.com*

**Department of Nuclear Medicine
Sofia Cancer Center
1, A. Saharov Blvd
1784 Sofia, Bulgaria
e-mail: sonya.sergieva@yahoo.com*