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High-resolution scintigraphy and ^{99m}Tc Bombesin are able to guide Mammotome biopsy and to detect lymph node invasion

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Abstract

High-resolution (HR) γ-ray detector ^{99m}Tc Bombesin (^{99m}TcBN) and ^{99m}Tc sestamibi (^{99m}TcSM), have been used to drive Mammotome biopsy after fusion of scintigraphic with digital X-ray images. We studied eight patients with class V microcalcifications. An HR detector with spatial resolution of 3 mm was matched with Mammotome biopsy system provided with Fisher digital X-ray device: images were fused to use the pointer indifferently on X-ray, scintigraphic and fused images. Fusion between X-ray and HR image has previously been reported. The 12 Mammotome samples/patient were weighted and counted in a well counter. Tumour/bkg (T/B) ratio was measured on HR images as well as on biopsy samples. Axilla was also explored with the portable HR device in order to diagnose node invasion. Conventional histology assessment and immunohystochemical study with anti BN receptor antibody was blindly performed on samples. All the patients studied with ^{99m}TcSM showed T1b cancer, ^{99m}TcBN detected one T1a and two T1b cancers. HR scan of axilla detected node metastases in two patients, both studied with ^{99m}TcBN. All the biopsies showed cancer on at least one of the 12 samples. Histology found node metastases in three patients: the two ^{99m}TcBN positive and one studied with ^{99m}TcSM whose axilla was negative at HR scan. Samples showed T/B ratio of 6.6 ± 0.4 for ^{99m}TcSM and 11.3 ± 0.9 for ^{99m}TcBN ($p < 0.01$). Note that also the patient with T1a cancer, showing 10.4 T/B ratio was included in the ^{99m}TcBN series. Not only ^{99m}TcBN HR is able to show breast cancer and to guide biopsy, but also detects node metastases. Our is the first ex vivo measurement of T/B ratio of ^{99m}TcBN on humans.

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Keywords: High-resolution scintigraphy; Breast biopsy; Scintillation detector; Image fusion; Mammotome system

1. Introduction

^{99m}Tc Bombesin (^{99m}TcBN) is a new radiotracer synthesised, labelled and produced as a sterile, apirogen KIT by the National. Research Center "Demokritos" for human use. After labelling, this tracer is taken up by Bombesin (BN) receptors (BNR) in vitro and in vivo [1,2]. Its behaviour does not biologically differ from the amphibian peptide[13Leu] BN. ^{99m}TcBN is apparently taken up by all BNR subtypes (BNS): actually ^{99m}Tc labels an amphibian peptide very similar to ancestral neurohormones from which the specialised peptides gastrin-releasing peptide (GRP) and neuromedin B (NMB) come by successive differentiation [1]. Mammalian peptides of the BN family, such as GRP or NMB, have their own BNS [3,4], which also take up the amphibian BN. Initial studies on humans have shown great ability of ^{99m}TcBN scintigraphy to detect breast and prostate cancers as well as small cell lung cancer, whereas other cancers, lung adenocarcinoma for example, were less frequently detected [2,5-7]. ^{99m}TcBN has shown ability to detect cancer with

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the technique of prone scintimammography, which is generally used with ^{99m}Tc sestamibi (^{99m}TcSM). This method, when used with ^{99m}TcSM has been shown to be suboptimal when it has to detect breast cancers sized less than 1 cm. [8]. High-resolution scintigraphy with breast compression showed much better results than Anger camera prone scintimammography in detecting breast cancer both with ^{99m}TcSM and ^{99m}TcBN [5,9,10]. Worth of note, high-resolution techniques as well as detectors showed substantial improvements in the last years [4,11]. At first it was not very clear why detection of small sized breast cancer was so difficult with prone scintimammography when using a radiopharmaceutical whose tumour/normal breast tissue uptake ratio (T/B) was considered as high as 9:1. Low resolution of Anger camera, distance from detector in prone position and the strong Compton field present at least at breast basis, in turn due to high muscular, cardiac and hepatic uptake of ^{99m}TcSM were studied as co-working causes for impaired detection [12–15]. The mentioned causes really work and lower T/B ratio on scintigraphic images. Actually breast compression and high-resolution scintigraphy obtain much better results than prone scintimammography [5,9,11,15], however source T/B ratio inside breast has been considered to be fixed at 9:1, phantoms to calibrate cameras were prepared considering a fixed ratio for large and small cancers, even though it is well apparent that uptake of ^{99m}TcSM depends on blood flow and oxidative metabolism [16], thus it changes with tumour growth and neo-angiogenesis [5,17]. Measurement of source T/B ratio simply has not been performed. Updated high resolution devices are now able to guide breast biopsy and to image cancer with precise detection of its relationship with normal neighbouring tissues. We studied the source T/B ratio of ^{99m}TcSM and ^{99m}TcBN on tumours smaller than 1 cm with Mammotome biopsy guided by high-resolution scintigraphy.

2. Equipment and method

2.1. High-resolution equipment

Present series was carried out with 1-in.^{2} IP-824 (Li-tech, Italy). IP-824 is a portable high resolution camera specially designed for radio-guided surgery. In the present study IP-824 was fitted to the biopsy window of Mammotome breast compressor: actually this window is square shaped and rather exactly as large as IP-824. Our HR camera can be inserted on the mechanical device that supports the mechanism of vacuum needle driver.

IP-824 consists of a square-hole tungsten collimator [18], a tungsten shielding housing and CsI(Tl) crystals directly inserted into the collimator holes. The crystal–collimator complex is coupled to position sensitive photomultiplier tube (PSPMT) [4]. Home-made charge readout electronics and a data acquisition system complete the detector.

The parallel square holed collimator is made of tungsten with 200 μm thick septa. The collimator is 26 mm × 26 mm large, exactly fitting the PSPMT size; each square hole is $3 \times 3\,mm^2$ wide and 30 mm long. Length of 30 mm results from apposition of two collimator blocks: first block, that includes crystals shows height of 6 mm. Adjunctive 24 mm block collimator is arranged on primary collimator + crystals integrated. Mechanical structure is made with high-precision methods and the final result is a compact collimator, with holes of the same size of crystals. The scintillator structure is composed of an 8×8 array of CsI(Tl) crystals (Spectra Physics-Hilger, UK). Crystals do not form an array by themselves, independently from the collimator: actually each single crystal exactly shows the dimensions of collimator holes. Crystals are covered by 100 μm of white reflective epoxy on their five blind surfaces. Crystals are 5 mm thick whereas the height of tungsten holes of first collimator block is 6 mm. The space remaining to reach the height of the first collimator module is filled with 1 mm of white epoxy. This technique allows perfect matching between collimator hole and crystal, with better signal noise ratio due to suppression of pattern mismatching and crosstalk among crystals.

Hamamatsu R8520-00-C12 PSPMT (Hamamatsu, Japan) shows overall area of $25.7 \times 25.7\,mm^2$ with a gain of about 3×10^6 at −800 V. The intrinsic charge spread of R8520 is lower than 0.5 mm FWHM. Spatial resolution depends directly on light spread and inversely on the square root of the number of photoelectrons coming from the photocathode. When light from a scintillation event in CsI(Tl) crystal strikes the PSPMT photocathode, an electron cloud is emitted, amplified by metal channel dynodes and collected on the six Y and six X wire anodes. These crossed wire anodes are used for position-sensitive function; charge readout electronics consists in standard resistive chain. The signals are sampled with a PCI-6110E National Instruments data acquisition board. The system is plugged into a PC (Pentium IV@3.0 GHz) via bus PCI full size. Data are processed for evaluation of maximum of samples signal, by each of the single 4 channels. The maximum count rate measured is about 50 kcount/s.

2.2. Mammotome biopsy

Biopsies were performed with a standard Mammotome device assisted by a Fisher digital X-ray stereotactic pointer. After having selected the biopsy field on the basis of standard X-ray mammography and after having compressed patient's breast, +15°, 0° and −15° digital images were acquired by Fisher system and transferred to Mammotome computer where the 0° image was fused with high-resolution scintigraphy (Fig. 1). The method of image fusion between scintigraphic and digital X-ray images (Fig. 2) has previously been reported [16].

We regulated the pointer of Fisher-Mammotome system in order to obtain vacuum biopsy samples of hot radioactivity spots.

This method did not create problems for sampling of micro-calcifications because of hot spot position, that