Combination of functional and anatomic images: high efficacy in oncological practice

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Purpose

Anatomical diagnostic modalities (conventional X-ray, CT, MRI) are established as the basic methods for diagnosis and staging of various malignant tumors. The main limitation of anatomical methods is their low sensitivity in diagnosis of early cancer which is not associated with remarkable structural changes.

At nowadays functional methods which are represented by PET and SPECT are often used as alternative of anatomical imaging: they are characterized by high sensitivity that can be explained by early onset of functional changes which are precede the structural burden of the organs. On the other side, problems with anatomical localization of abnormalities, moderate specificity, low anatomical resolution are well known weaknesses of functional modalities.

It can be assumed that effective combination of anatomical and functional information can significantly improve accuracy of final conclusion and increase efficacy of diagnostic strategy.

In this study we evaluate possible gains of these combinations in patients with breast, lung cancer and cancer patients evaluated for bone metastases.
Methods and Materials

1. We studied 123 consecutive patients with clinical suspicion for breast cancer (BC). SPECT was performed 15 min after i/v injection of 740-860 MBq of 99mTc-sestamibi on side opposite the suspected abnormality. Data were acquired with low-energy high-resolution (LEHR) collimators in 128 projections of 15s each over 360° on 128 # 128 pixel matrix. Images with focal, multifocal and diffuse abnormal tracer uptake were scored as abnormal. Focal areas of tracer accumulation in axial region were considered as signs of lymph node metastases (LN). Ultrasound (US) examinations were performed using multifrequency (10-14MHz) linear probe. Following signs were considered abnormal: hypoechoic mass, irregular morphology, poorly defined edges, inhomogeneous echo structure, posterior acoustic attenuation. Axillary lymph nodes (LNs) with more than 10mm in maximum transverse dimension, or an absent hilum were considered abnormal. All breast lesions and LNs were verified by biopsy and follow-up or by operation.

2. We also examined 91 patients with non-small cell lung cancer (NSCLC). SPECT with 99mTc-sestamibi was performed after conventional staging all of them. Acquisition on dual head camera was started 15 min after i/v injection of 740 MBq of 99mTc-sestamibi. SPECT images of the chest were acquired using the following parameters: matrix size 128x128, time per view 15s, degrees of rotation 180°, number of views 64 and continuous mode with noncircular orbit. Helical CT data were acquired with exposure of 100mAs, 120kV, pitch of 1,2 and collimation of 4mm with rotation time 0,75s. Images were reconstructed with a thickness of 1,5mm. LN stations were evaluated and allocated into one of nine groups, according to the LN map definition for lung cancer staging proposed by Mountain in 1997. All LNs with abnormal radiotracer uptake were considered positive. LN assessment on CT image was based on LN size with short axis diameter of >10mm defined as abnormal. Diagnostic results of SPECT, conventional CT alone and SPECT-CT staging were validated by histological examinations of operation material.

3. In 161 patients with different types of malignant tumor we analyzed diagnostic value of SPECT/CT and whole-body planar bone scintigraphy (BS) with $^{99m}$Tc-methylene diphosphonate (MDP). Whole-body planar bone scintigraphy (WB) and SPECT/CT images were obtained 3-4h after i/v injection of 740 MBq of 99mTc-MDP in dual-head SPECT-CT device with LEHR collimators (scanning speed of 10 cm/min, matrix size 128x128, time per view 20s, degrees of rotation 180°, number of views 64 and continuous mode with noncircular orbit). The CT part of examination was performed as diagnostic CT acquisition with 120kV, 70-80 mA, rotation time 0,7s, pitch 3mm, and 5mm slice thickness. BS image was considered metastatic when a patient had one or few areas of uptake that could not be differentiated as a benign lesion, such as joint damage or trauma. The final diagnosis relating to an area of uptake was made depending on the findings of the SPECT/CT study. Lesions were classified as malignant when the sites of increased
99mTc-MDP uptake were associated with characteristic morphological changes on the CT images or when we detected progression of the changes during follow-up.
Results

In the whole group of evaluated women with suspicious for breast cancer both US and breast scanning (MSC) were characterized by high sensitivity, specificity and accuracy (98%, 96%, 97%) mainly because of prevalence of large (2 cm and more) lesions.

In 36 women with lesions below 1 cm SMG revealed 12 of 14 cases of BC (fig. 1) and refused malignancy in 16 of 21 women's with benign breast lesions. Sen, Sp and Ac of SMG in this group was as follows: 86%, 76% and 80%. US examinations in this group diagnosed benign lesions in 27 of 35 evaluated women: 21 - true negative, 6 - false negative. In remaining 8 cases US signs of BC were true positive. In women with lesions below 1 cm US characterized by low Sen (57%), high Sp (100%) and moderate Ac (82%).

Taking into account that SMG represents functional and US - anatomical information about breast lesions we tested diagnostic value of their combination (US+SMG). BC was diagnosed in the case if either SMG or US revealed abnormalities. This diagnostic strategy was characterized by outstanding Sen (100%), moderate Sp (76%) and Ac (82%).

Scintigraphic signs of LN metastases (fig. 2) revealed in 40 patients: 23 - true positive, 17 - false positive. Among 58 women with normal AxSc results 8 had LN metastases and 40 - uninvolved nodes. Sen, Sp and Ac of MSG were as follows: 74%, 75% and 74%.

Sonography diagnosed LN metastases in 44 women: 30 were metastatic on histology while other 14 - uninvolved. On the contrary, 8 of 47 US normal sized nodes were metastatic on histology. US had following values when used for diagnosis of axillary LN metastases: Sen - 79%, Sp - 77%, Ac - 77%.

When LN metastases were diagnosed as the combination of concordantly abnormal US and AxSc examinations Sp reached 96%, Sen dropped down to 52% and Ac - 79%. Another model was based on the assumption that LN metastases must be diagnosed in all patients with abnormal US or AxSc examinations. According to this strategy Sen reached 87%, Sp - 68% and Ac - 78%.

Possible diagnostic strategies based on combination of MSG and US are presented on figures 3, 4, 5.

According to histological verification 35 of 91 evaluated patients had LN invasion by NSCLC. SPECT detected LN involvement (pic. 6) in 24 of these 35 patients and was false positive in additional 16 patients. Sensitivity (Sen), specificity (Sp) and accuracy (Ac) of SPECT in diagnosis of LN invasion by NSCLC was as follows: 69%, 59%, 63%.
Diagnostic accuracy of CT for detection of LN involvement was inferior (pic. 7) to SPECT: Sen - 59%, Sp - 53%, Ac - 55%.

Combination of SPECT and CT data offer interesting diagnostic solution. If LN involvement is detected by at least one of these methods Sen reached 88% with corresponded Sp -43%, Ac - 56%. This strategy can be used for discrimination of patients that can be treated by operation or radiosurgery and those who need further invasive diagnostic procedures (pic. 8).

Another interesting solutions can be achieved in patients without CT signs of atelectasis and pneumonia. In this group concordant changes on SPECT and CT are characterized by high Sp (97%) with low Sen (55%) and moderate Ac (81%). It can be assumed that abnormalities in regional LN diagnosed on both CT and SPECT images in patients without atelectasis and pneumonia can be interpreted as tumor invasion (pic. 9).

SPECT-CT was performed in 161 cancer patients who we referred for routine bone scanning.

The first group was formed by 74 patients with equivocal results of whole body planar imaging. SPECT-CT data clarified final diagnosis in 93% cases. Most patients had nonspecific changes (pic 10, 13) which were determined in 49 cases (66% of equivocal changes): 49% - degenerative disease 10% trauma, 7% others (enchondromas, infarcts, etc.)

Metastatic character of lesions determined in 20 patients (27% of equivocal changes).

Second group was represented by 87 consecutive patients with normal results of planar whole body scintigraphy. During SPECT-CT examination metastatic lesions (pic. 11) revealed in 8 (9%) of this 87 patients. We proposed following diagnostic strategy for combination of conventional bone scan and bone SPECT-CT (pic. 12).
Fig. 1: Increased accumulation of 99mTc-MIBI in 9mm lesion which was diagnosed on histology as breast cancer.

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Fig. 2: Increased accumulation of 99mTc-MIBI in non-enlarged ovoid axillar lymph node which was diagnosed on histology as breast cancer metastases.

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Fig. 3: Diagnostic algorithm for patients with negative findings on scintigraphy and axillary US.

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Fig. 4: Diagnostic algorithm for patients with positive findings on scintigraphy or axillary US.

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Fig. 5: Diagnostic algorithm for patients with positive findings on scintigraphy and axillary US

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Fig. 7: Accumulation of 99mTc-MIBI in non-enlarged lymph node which was diagnosed on histology NSCLC metastases.

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**Fig. 6:** Accumulation of 99mTc-MIBI in metastatic lymph nodes in patient with NSCLC.

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**Fig. 8:** Decision tree for patients without SPECT and CT signs of metastatic lymph node involvement by NSCLC

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Fig. 9: Decision tree for patients without atelectasis/pneumonia and with SPECT plus CT signs of metastatic lymph node involvement by NSCLC

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Fig. 10: A 50-year-old female patient with breast cancer. 99mTc MDP bone scintigraphy images show a single area of focal uptake radiotracer in the L2 vertebral body which was considered as probably malignant lesion (a). 99mTc MDP SPECT/CT images (b) show degenerative and posttraumatic changes in the area of increase tracer uptake.

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Fig. 11: A 56-year-old male patient with lung cancer. 99mTc MDP SPECT images (a) show normal distribution radiotracer without focal uptake. CT images (b) shows lytic lesion in the Th7 vertebral body which was classified as malignant

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Fig. 12: Diagnostic strategy for routine whole body bone scintigraphy in combination with SPECT-CT.

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Fig. 13: A 50-year-old female patient with breast cancer. 99mTc MDP bone scintigraphy images show a single area of focal uptake radiotracer in the L2 vertebral body which was considered as probably malignant lesion (a). 99mTc MDP SPECT/CT images (b) show degenerative and posttraumatic changes in the area of increase tracer uptake.

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Conclusion

In patients with cancer combination of anatomical and functional information can significantly improve accuracy of staging procedures. SPECT-CT must be considered as very promising diagnostic technique.
References

No references