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Improved detection of melanoma metastases by iodine maps from dual energy CT

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ABSTRACT

Objective: Metastatic disease in melanoma has an unpredictable nature with deposits in rare locations such as musculature. Dual energy CT (DECT) provides high contrast-visualization of enhancement by using spectral properties of iodine. Purpose of this study was to evaluate whether iodine maps from DECT improve lesion detection in staging examinations of melanoma patients.

Methods: This retrospective study was approved by IRB and written informed consent was obtained from all patients. 75 contrast-enhanced DECT scans (thorax and abdomen) from 75 melanoma patients (n = 69 stage IV; n = 6 stage III) were analysed. For each patient, conventional CT and iodine maps were reviewed independently by two radiologists. The number of lesions detected by reviewing the iodine maps following conventional CT was recorded. Unweighted Cohens Kappa coefficient (κ) was used for concordance analysis, Wilcoxon test for comparing lesion detection rates.

Results: In 26 patients, at least one reader found additional lesions on iodine maps (inter-reader agreement 89%, $\kappa = 0.74$ (0.742–0.747)). Compared to grey-scale images, mean detection rate for metastases improved from 86% (range 82–90) to 94% (90–99%) ($p \leq 0.01$), for muscle metastases from 8% (8-8%) to 99% (98–100%) ($p \leq 0.06$). Findings included 2 pulmonary emboli.

Conclusion: Iodine maps from DECT improve detection of metastases, especially muscle metastases, and relevant findings in staging examinations of melanoma patients.

1. Introduction

A dramatic increase in incidence of malignant melanoma can be observed in the western world, reaching incidence rates of epidemic levels [1,2]. Malignant melanoma is an aggressive disease with an unpredictable biological behaviour. Metastases affect nearly all tissues [3], including sites rarely seen in other solid tumours [4].

The most common staging system refers to the American Joint Committee on Cancer (AJCC). Depending on the anatomical site of the distant metastases (skin, subcutaneous tissue, distant lymph nodes vs lung vs all other sites) and the serum level of lactate dehydrogenase enzyme, the M stage is delineated into three categories, associated with different one-year survival rates [5].

A study with 589 patients suffering from stage IV melanoma found a dependence of patient survival times on the number of metastases [6], which is not included in the AJCC staging system due to limitations of diagnostic accuracy of imaging tests during data acquisition of the referenced multicentre study [5]. This reflects the importance of an accurate radiological assessment of every lesion, including those in typical "blind spots" like skeletal musculature [7]. Muscle metastases are, compared to other tumour entities, common in melanoma, occur typically without initial clinical symptoms [8] and are difficult to detect due to the large volume that they can be distributed in, their initial small size and their similar CT density compared to muscles.

The standard imaging modality for melanoma staging is CT. Compared to positron emission tomography (PET) or magnetic resonance imaging (MRI), CT is fast and less expensive. Dual energy computed tomography (DECT) is a promising development in CT technology using two x-ray spectra. Based on the different atomic numbers of soft tissues and contrast agent and the associated spectral properties, a material differentiation is possible, which enables multiple clinical benefits [9–11]. In oncological imaging, DECT has been found valuable in the assessment of liver and kidney masses [12,13], of pulmonary nodules [14] and in therapy monitoring [15–17].

Abbreviations: DECT, dual energy CT.

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Table 1
Applied amount of contrast agent (Imeron 300, Bracco, Konstanz, Germany).

Body weight [kg]	Volume contrast agent [ml]	Flow rate [ml/s]
<55	85	3.1
55–65	115	3.5
65–90	130	4
>90	145	4.5

In this study we use iodine maps calculated from DECT by using the different spectral properties of iodinated contrast agent and the surrounding tissue. Iodine maps highlight enhancing lesions like melanoma metastases known to be hyper-arterialised and visualize their spatial contrast agent distribution. To the best of our knowledge, the potential of iodine maps for lesion detection in melanoma staging examinations has not been investigated yet.

The purpose of this study was to evaluate whether iodine maps improve lesion detection in staging examinations of melanoma patients.

2. Materials and methods

2.1. Patient population

This retrospective study was approved by the institutional review board and written informed consent was obtained from all patients. Over a period of 4 months (November 2014–February 2015) 75 contrast enhanced dual energy scans from 75 melanoma patients (n = 69 stage IV and n = 6 stage III following AJCC classification) were evaluated. Mean age of patients was 61 years (range 27–86), including 32 female (mean age 58 years, range 35–81) and 43 male (mean age 63, range 27–86) patients.

Inclusion criteria were

- Patient with histologically proven malignant melanoma.
- Protocol parameter as described in the following paragraph. This protocol is the standard for staging examinations of melanoma patients in our department. Patients examined with a modified protocol (for example without contrast agent because a severe allergic reaction had been reported) were excluded.

2.2. CT examination and image post-processing

Spiral image acquisition was performed on a second-generation 2×64-slice dual source dual energy CT (Siemens Somatom Definition Flash, Siemens AG, Forchheim, Germany), using two different tubes voltages (100 kV and tin filtered 140 kV, reference tube currents 185/143 mAs for thorax and 200/155 mAs for abdomen respectively). The scan was acquired with online dose modulation (CARE Dose 4D, Siemens AG, Germany) and a detector collimation of 32×0.6 mm.

Examination protocol included intravenous application of non-ionic iodinated contrast agent (Imeron 300, Bracco, Konstanz, Germany) with a body weight adapted amount and flow rate (Table 1) via an automated injector. Triggering contrast agent injection was realized by attenuation measurements in a region of interest (ROI) placed in abdominal aorta on the level of the liver hilum. Arterial phase started 10 s after the cut off value of 120 HU was detected (Bolus-tracking technique) with a caudocranial scanning direction and a pitch value of 0.9. Scan field of view (FOV) was from neck to the caudal margin of the liver. Portal venous images were acquired 60 s after arterial phase in craniocaudal scanning direction with a pitch value of 0.6. Scan FOV was from diaphragm to proximal part of upper thigh.

With a weighting factor of 0.5 the two datasets from the two x-ray tubes were fused to virtual images corresponding to a 120 kV scan (in the following these images will be referred to as "conventional grey scale CT") and were reconstructed into axial 3 mm slices using a standard soft tissue reconstruction kernel (D20f smooth). For lung parenchyma additional axial 1 mm slices were reconstructed using a standard very sharp reconstruction kernel (B70f very sharp).

DECT data from both x-ray tubes were also transferred to a dedicated workstation. With a commercially available software tool (SyngoMMWP VE36A, Siemens AG, Berlin and Munich, Germany), the spectral information from dual energy data was used to generate iodine maps in axial 3 mm slices (for lung parenchyma additional 1 mm slices). These maps are comparable to colour coded CT images, but the displayed voxel values base exclusively on materials identified by the algorithm as contrast agent. An overlay of iodine map and conventional CT was exported to the picture archiving and communication system (PACS, GE Healthcare, Barrington, IL, USA) used in clinical routine.

2.3. Data analysis

Two radiologists (4 and 3 years of experience in oncological imaging) assessed the examinations independently on the PACS system. Both radiologists reported the number, localization and dignity of all lesions additionally detected by reading the iodine maps after analysing the conventional grey scale CT. To take into account eventual false positive findings, they also stated if the additionally diagnosed lesions could retrospectively be identified on the conventional grey scale CT. The radiologists were free to adjust the windowing settings.

The software algorithm creating iodine maps is optimized to highlight enhancing lesions, but not to delineate anatomical structures in all detail. Consequently goal of this study was to evaluate, if grey scale CT with complementary iodine maps can improve lesion detection rate compared to reading exclusively grey scale CT. In a clinical setting, iodine maps would rather supplement than replace conventional grey scale CT. With respect to these considerations, we did not determine the false negative rate of reading exclusively iodine maps without grey scale CT.

Some metastases were not proven histologically. Classification of not pathologically assessed lesions as metastases was therefore based on commonly accepted imaging criteria including invasion of surrounding tissue, rapid growth on subsequent or in review of prior examinations, contrast enhancement, necrosis or diffuse/infiltrative lesion margins (example: a new enhancing tumour of the adrenal gland in a patient with stage IV melanoma is probably a metastasis). Furthermore, imaging findings were recorded, comparable to a standard radiological report. These lesions included pulmonary emboli, typical benign lesions like renal cysts and liver haemangioma as well as lesions not unequivocal benign or malignant. The reference standard ("goldstandard") for calculating the detection rates was the total number of lesions per scan, defined as the sum of all lesions detected on conventional CT and on iodine maps by both readers.

For statistical analysis, continuous variables were expressed as means (with range between readers). For categorical data, distribution is given as percentage per category. Unweighted Cohens Kappa coefficient (κ) was used for concordance analysis, Wilcoxon test for comparing lesion detection rates (MATLAB 2015a, The MathWorks, Inc., MA, USA). The statistical significance level was set to 0.05 for all analyses. Dose calculations of DECT examinations were based on the computed tomography dose index (CTDI) and the dose length product (DLP), reported as mean and standard deviation.