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Performance and clinical impact of machine learning based lung nodule detection using vessel suppression in melanoma patients

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ABSTRACT

Purpose: To evaluate performance and the clinical impact of a novel machine learning based vessel-suppressing computer-aided detection (CAD) software in chest computed tomography (CT) of patients with malignant melanoma.

Materials and methods: We retrospectively included consecutive malignant melanoma patients with a chest CT between 01/2015 and 01/2016. Machine learning based CAD software was used to reconstruct additional vessel-suppressed axial images. Three radiologists independently reviewed a maximum of 15 lung nodules per patient. Vessel-suppressed reconstructions were reviewed independently and results were compared. Follow-up CT examinations and clinical follow-up were used to assess the outcome. Impact of additional nodules on clinical management was assessed.

Results: In 46 patients, vessel-suppressed axial images led to the detection of additional nodules in 25/46 (54.3%) patients. CT or clinical follow up was available in 25/25 (100%) patients with additionally detected nodules. 2/25 (8%) of these patients developed new pulmonary metastases. None of the additionally detected nodules were found to be metastases. None of the lung nodules detected by the radiologists was missed by the CAD software. The mean diameter of the 92 additional nodules was 1.5 ± 0.8 mm. The additional nodules did not affect therapeutic management. However, in 14/46 (30.4%) of patients the additional nodules might have had an impact on the radiological follow-up recommendations.

Conclusion: Machine learning based vessel suppression led to the detection of significantly more lung nodules in melanoma patients. Radiological follow-up recommendations were altered in 30% of the patients. However, all lung nodules turned out to be non-malignant on follow-up.

1. Introduction

Lung nodule detection on chest computed tomography (CT) examinations is a common task for radiologists. Besides screening for primary malignancies of the lung, lung nodule detection is important when searching for metastatic disease in cancer patients. Various reasons such as fatigue, distraction or satisfaction of search can lead to missed lung nodules [1,2].

In melanoma patients, pulmonary metastatic disease worsens prognosis and detection of pulmonary metastases can alter treatment [3–6]. Therefore, an accurate and reliable detection of metastases in CT examinations of melanoma patients is important.

Previous computer aided detection (CAD) - systems were based on intensity-based schemes, template-based approaches and machine learning classifiers [7–11]. The benefit of these CAD systems in the detection of sub-solid and solid lung nodules has been demonstrated [12–15]. However, commercially available CAD systems can lead to a substantial amount of false positive findings [16,17] and can be

Abbreviations: AJCC, American Joint Committee on Cancer; CAD, computer-aided detection; CT, computed tomography; GGO, ground glass opacities; HU, Hounsfield units; ROI, region of interest; SOP, standard operating procedures

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confounded by several factors like inadequate breath hold.

A recently introduced machine learning based CAD system produces additional axial CT images with suppressed pulmonary vessels to enable easier and more comprehensive detection of lung nodules [18]. The additional vessel-suppressed reconstruction is stored in the Picture Achieving and Communication System (PACS) and can be reviewed by the radiologist alongside the regular CT examination.

We sought to evaluate this novel post processing machine learning based CAD-system using vessel suppression (ClearRead CT, Riverain Technologies, Miamisburg, OH) for the detection of pulmonary nodules in the follow-up chest CT of melanoma patients.

2. Material and methods

2.1. Patients

Our retrospective study was approved by the local ethics committee (Reference number: 5658). We performed a retrospective search in the institutional PACS (Sectra Medical Systems GmbH, Linköping, Sweden) for melanoma patients that underwent a chest CT examination on one of our institutional CT scanners between 01/2015 and 01/2016 (further referred to as index CT). All consecutive 46 patients that met the inclusion criteria were included in our study, there were no exclusions.

2.2. Clinical data

Clinicopathological data of all patients were obtained from the electronic clinical and histological records by one of the coauthors (BJ) who was blinded to the radiological data. Clinical and histological data included primary tumor localization, melanoma subtype (superficial spreading melanoma, acral lentiginous melanoma, lentigo maligna melanoma, nodular melanoma and others), vertical tumor thickness (Breslow's depth), Clark level, therapeutic treatment, tumor spread at the initial tumor staging, at the index staging and at the last follow up [19–22].

The anatomic stage groupings from I to IV according to the TNM staging system developed by the American Joint Committee on Cancer (AJCC) were extracted from the electronic clinical reports [22].

2.3. Image acquisition

The CT examinations were performed on a 128-row CT scanner (Somatom Definition Flash, Siemens Healthineers GmbH, Forchheim, Germany) according to the institutional standard operating procedures (SOPs). Scanning was performed with automated tube potential selection (CarekV, preset: 100 kVp, Siemens Healthineers) and tube current modulation (CareDose4D, Siemens Healthineers, reference mAs: 87 mAs). Rotation time was 0.28 s and collimation was 0.6 mm in all scans. The scan volume included the supraclavicular space and reached to the mid-level of the liver. Thus, the complete lung parenchyma was assessed in all scans. All scans were performed with contrast material (Imeron 400, Bracco Imaging Deutschland GmbH or Accupaque 300 mg, GE Healthcare Buchler GmbH & Co) which was adapted to patient weight (Imeron 400: 0.8 ml/kg patients weight; Accupaque 300 mg: 1 ml/kg patients weight). All scans were performed in supine position in inspiration after an automated breath-hold command. The CT scan was started using automated bolus triggering technique. A region of interest in the descending aorta with a threshold of 120 Hounsfield Units was used to start the arterial phase CT scan in all scans.

2.4. Image reconstruction

Axial images were reconstructed with 1 mm and 2 mm slice thickness using a sharp kernel (B70f) and a lung window (window level: −500, window width: 1500). Additional reconstructions included axial 2 mm slices with medium levels of iterative reconstruction (I31f, Safire level 3, Siemens Healthineers) and 3 mm coronal and sagittal reconstructions (B70f). A machine learning based CAD system (ClearRead CT, Riverain Technologies, Miamisburg, OH) was used to reconstruct vessel-suppressed axial 1 mm images. The CAD system uses an acquisition normalization which includes several steps. Initially, an anatomic segmentation is performed. Afterwards vessel suppressed axial images are reconstructed. Additionally, the CAD system performs automated nodule detection and nodule characterization which is provided as a report in the PACS. [18]. All reconstructions were transferred to the PACS system.

2.5. Image interpretation

Three radiologists with 6 years (AJ, board certified), 6 years (SB, board certified) and 5 years (BJ, resident) of experience in reading chest CT independently reviewed all pseudonymised original CT reconstructions. A maximum of 15 lung nodules per patient were reviewed. For each lung nodule the readers recorded the image number, the anatomical location, the longest nodule diameter on axial images (in mm) and the density (in Hounsfield Units, HU) which was measured by region of interest (ROI) settings. MIP reconstructions were allowed for reading. Lesions were classified as solid or ground glass lesions. Using coronal and sagittal reconstructions for lung nodule detection was to the discretion of the readers. There was an interval of at least six weeks between the original CT and the CAD reading sessions.

Afterwards, the vessel-suppressed CAD reconstructions were reviewed by AJ (board certified radiologist with 6 years of experience in chest CT). In this session, the findings of all readers were brought together. The findings in the vessel-suppressed CAD images were compared to the findings detected on the original CT images for final analysis.

All nodules detected in the CAD reconstruction but not in the original CT reconstruction were classified as false positive, therefore we only rated missed nodules which were also present in the original images.

2.6. Outcome analysis

Composite outcome included follow-up chest CT examinations and clinical follow-up (pathology reports, surgery reports, notes from outpatient hospital visits or readmissions and available physician letters). The impact of the additional lung nodules detected with CAD on radiological follow-up recommendations and on clinical management was assessed by two of the coauthors (BJ, clinical dermatologist, 3 years of experience; AJ, board certified radiologist with 6 years of experience). For follow-up recommendations, nodules were classified as “benign”, “indeterminate” and “highly suspicious for metastasis” and follow-up recommendations were noted. On the analyzed images, the following radiological criteria were used to characterize lung nodules: Nodule size of 6–8 mm or smaller without solid components or with calcifications was rated as benign. Nodule size of > 8 mm with solid components was rated as highly suspicious for metastasis. Nodule size < 8 mm with solid components or sub-solid components was rated as indeterminate.

All missed nodules were reviewed by AJ, a board certified radiologist with 6 years of experience on follow up CT imaging to asses lung nodule dignity. Size changes on follow up CT in patients undergoing systemic treatment were rated as malignant. In patients without systemic treatment lung nodule growth was considered as a sign of malignancy.

2.7. Statistical analysis

All data are given in mean ± standard deviation. Data analysis was performed using IBM SPSS Statistics 22™ for Windows (SPSS, Chicago, IL, USA). Statistical significance was set to $p < 0.05$. A Kolmogorov-