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# Dual-energy CT can detect malignant lymph nodes in rectal cancer

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ABSTRACT

*Background:* There is a need for an accurate and operator independent method to assess the lymph node status to provide the most optimal personalized treatment for rectal cancer patients.

This study evaluates whether Dual Energy Computed Tomography (DECT) could contribute to the preoperative lymph node assessment, and compared it to Magnetic Resonance Imaging (MRI).

The objective of this prospective observational feasibility study was to determine the clinical value of the DECT for the detection of metastases in the pelvic lymph nodes of rectal cancer patients and compare the findings to MRI and histopathology.

*Materials and methods:* The patients were referred to total mesorectal excision (TME) without any neoadjuvant oncological treatment. After surgery the rectum specimen was scanned, and lymph nodes were matched to the pathology report.

Fifty-four histology proven rectal cancer patients received a pelvic DECT scan and a standard MRI.

The Dual Energy CT quantitative parameters were analyzed: Water and Iodine concentration, Dual-Energy Ratio, Dual Energy Index, and Effective Z value, for the benign and malignant lymph node differentiation.

*Results:* DECT scanning showed statistical difference between malignant and benign lymph nodes in the measurements of iodine concentration, Dual-Energy Ratio, Dual Energy Index, and Effective Z value.

Dual energy CT classified 42% of the cases correctly according to N-stage compared to 40% for MRI.

*Conclusion:* This study showed statistical difference in several quantitative parameters between benign and malignant lymph nodes. There were no difference in the accuracy of lymph node staging between DECT and MRI.



## 1. Introduction

There is a need for more accurate methods for preoperative staging of rectal cancer to determine the optimal treatment. It is essential to identify poor prognostic features, such as lymph node involvement in the selection of patients for trans-anal endoscopic microsurgery (TEM) or TME with or without neoadjuvant treatment [1,2].

MRI is the standard method used for the assessment of lymph nodes in rectal cancer [3]. It has shown a sensitivity of 50–80% [4]. The results vary significantly from one center to another. Other modalities have been introduced to assess the lymph nodes. PET-CT has demonstrated moderate results with a sensitivity of 66% [5], as has trans rectal ultrasound (TRUS) with a reported sensitivity of 67–93% [6]. Elastography has also shown promising results in lymph node assessment [7]. Hence efforts are made to find better techniques for the evaluation of lymph node involvement in rectal cancer. DECT was invented in the 1970s, but only recent development allowing for sufficient tube currents at low voltages has made it interesting in a broader clinical application. It is a new technique that allows differentiation of materials and tissues based on CT density values derived from two synchronous CT acquisitions. With the development of the latest new dual energy CT systems, this technique can now be used routinely in abdominal imaging [8,9].

DECT x-rays are produced by the rapid switching of high- and low- voltages tubes which allows precisely captured data for creating accurate material decomposition images (e.g., water, and iodine

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based material decomposition). In addition, it provides monochromatic images with energy levels ranging from 40 to 140 KeV. The material decomposition images can be utilized to estimate the quantity of, for example water and iodine content, in regions of interest. One could hypothesize that this might enable differentiation between malignant and benign lymph nodes. Furthermore the monochromatic images, provides information about the attenuation changes of different materials as a function of x-ray photon energy [10–13]. DECT provides quantitative measurements based on mathematical algorithms from the x-rays interaction with certain materials, giving a more objective and non-operator dependent evaluation than MRI and TRUS.

The purpose of this study is, to determine the clinical value of the DECT for the detection of metastases in the pelvic lymph nodes of rectal cancer patients and compare the findings to MRI and histopathology.

## 2. Materials and methods

### 2.1. Patients

Lymph nodes from fifty-four consecutive patients underwent prospective evaluation with DECT, MRI and histopathology. The inclusion criteria were the presence of histo-pathologically verified adenocarcinoma of the rectum, with MRI findings of T stage 1, 2 or 3 with <5 mm depth of extramural invasion and with no evidence of tumor within 1 mm of the mesorectal fascia. These patients are, in our institution, candidates for surgical treatment without neoadjuvant radio-chemo therapy.

All patients, including 29 male patients (53–91 years; mean 71.9 years) and 25 female patients (53–93 years; mean 72.2 years) had a clinical suspicion of rectal cancer during colonoscopy. The diagnosis was verified histo-pathologically, and the patients were preoperatively staged with a CT scan of the abdomen and thorax to determine the M-stage, and MRI of the pelvis to determine the T and N- stage. All patients received a total mesorectal excision.

### 2.2. Image analysis

#### 2.2.1. Dual energy CT in vivo

All the patients underwent a preoperative DECT scan. Patients were placed in the supine position. Patients were injected with iodine based contrast agent (Omnipaque 300; GE healthcare) at a flow rate of 3 mL/s, to an amount of 1.0 mL per kilogram. It was injected intravenously before the scanning. The dual-energy scans were covering the pelvis to detect pelvic lymph node involvement. CT was performed with a high definition CT scanner (GE discovery CT750 HD, GE Healthcare®, Milwaukee, WI). Using the spectral imaging scan mode with fast tube voltage switching between 80 and 140 kVp from view to view. The spectral imaging acquisition protocol for abdomen was used: 600 mAs; helical scan with pitch, 0.984:1; rotation time, 1.0 s; collimation thickness, 0.625 mm × 64; reconstruction field of view, 30 cm. Typically, the average computed tomography dose index volume is 32.01 mGy. Based on the acquired raw imaging data, the iodine- and water-based material decomposition images and 101 sets of monochromatic images with energy ranges from 40 to 140 KeV were reconstructed and analyzed with integrated imaging analysis tools for quantitative assessment [14].

(GSI Viewer software 4.4, GE Healthcare®, Waukesha, Wisconsin).

Quantitative parameters included the following: (a) Iodine and water concentrations (mg/mL) in lymph nodes. (b) Dual-Energy ratio (c), dual energy index (d) and Effective Z. Using imaging tools, the effective-z, water- and iodine- concentration were determined and the average were calculated. The dual energy ratio, a surrogate measure of the slopes of the HU curves, expressing the material attenuation against x-ray photon energy, and calculated by the CT attenuation difference at 50 and 140 KeV, divided by the energy difference (90 Kev) from the HU curve: $[\text{lambda}]_{HU} = (HU_{50kev} - HU_{140Kev})/90$. The difference in x-ray attenuation at two different photon energies were characterized by the dual energy index: $DEI = (HU_{80kev} - HU_{140Kev})/(HU_{80kev} + HU_{140Kev} + 2000)$.

For each lymph node, one region of interest (ROI) was defined in each slice. ROIs were drawn as big as possible to cover most of the nodular region. A senior abdominal radiologist (ML), blinded to the diagnosis drew the ROIs.

#### 2.2.2. Dual energy CT ex vivo

After the TME, the fresh mesorectal specimens were scanned ex vivo on a clinical DECT scanner (GE discovery CT750 HD, GE Healthcare, Milwaukee, WI). For settings see Ref. [14].

Immediately after scanning, all the specimens were photographed and lymph nodes were individually numbered according to their position on the photograph and on the scanning image (Fig. 1). In this way a meticulous lesion-by-lesion analysis was performed. Two experienced pathologists, blinded to the radiologic and surgical findings, reviewed the pathological results and qualified immune-histochemical findings as of benign or malignant.

#### 2.2.3. MRI imaging in vivo

Evaluation of the lymph nodes on MRI images was performed by a senior abdominal radiologist, from the department of radiology in our hospital. The criteria used for a malignant lymph node were as defined by Brown et al. based on the size, signal intensity and border contour [15]. Size above 5 mm, mixed signal intensity and irregular lymph node border were parameters to predict malignancy.

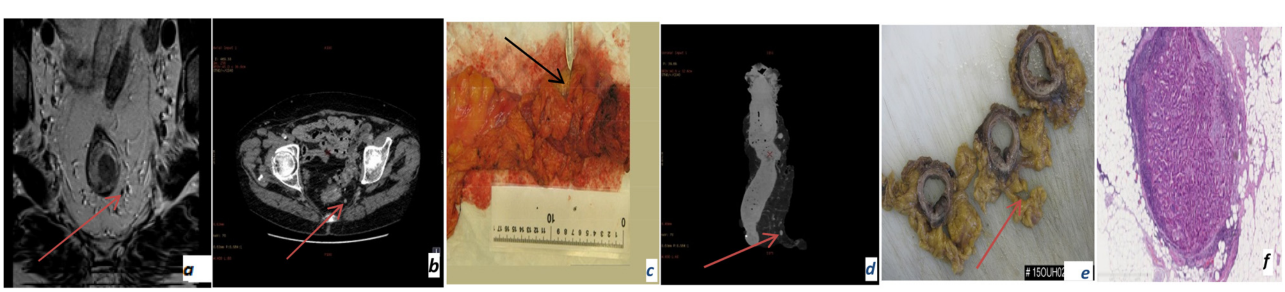


**Fig. 1.** Individual lymph node matched from image A to E.
Image A represents the preoperative MRI scanning. The lymph node of interest is marked with an arrow. Image B represents the preoperative DECT scanning. The lymph node of interest is marked with an arrow Image c represents the rectal specimen. The same lymph node is marked with an arrow. Image D is the same lymph node seen on the specimen DECT scan. Image E is the isolation of the same lymph node followed from preoperative scan to specimen photograph and further to the specimen scan. Image F is the histological validation.