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**Dual-energy computed tomography iodine maps of tissue perfusion:
A dose-reduced alternative to pancreatic computed tomography perfusion**

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Functional imaging methods are of increasing importance for medical imaging, as improvements in diagnosis, therapy planning, and personalized treatments are based on quantitative biomarkers. In contrast to current morphological imaging, information on tissue physiology provided by functional imaging methods can serve as a reliable, reproducible and quantitative measurement of patient pathology. Therefore, functional imaging methods could be used as quantitative imaging biomarkers for therapy response assessment, individualized therapy decisions or drug development. Compared to currently used techniques, like biopsies, imaging biomarkers are non-invasive, more flexible, easily reproducible and could be readily integrated into the clinical workflow.

Computed tomography (CT) is well suited for the development of quantitative imaging biomarkers because of the inherently quantitative image acquisition and the high reproducibility. The functional imaging method of CT perfusion, which allows for the measurement of tissue perfusion with a dynamic acquisition of an injected contrast agent bolus, has already shown promising results for the use as an imaging biomarker in abdominal tumors. Despite a large number of encouraging studies for the application of CT perfusion for abdominal tumors, it has not yet been adopted into clinical routine. Current acquisition protocols are associated with a comparatively high patient radiation exposure, impeding everyday clinical use.

Dual-energy computed tomography (DECT) on the other hand allows for quantitative material decomposition and has also shown promising results for the examination of abdominal tumors using DECT iodine maps, which quantify the concentration of an iodinated contrast agent. However, the application of DECT iodine maps to the measurement of tissue perfusion (as a dose-reduced alternative to CT perfusion) has not been researched in detail yet.

Therefore the main goal of this thesis was the quantitative assessment of DECT iodine maps of tissue perfusion. For this purpose, DECT iodine maps were quantitatively compared against CT perfusion maps, using the pancreas as an example for the abdominal organs.

As a first step, two commonly used models for CT perfusion were implemented in in-house developed software to allow for truly quantitative evaluation, validating the implementation against a digital perfusion phantom. Furthermore, as a prerequisite for the calculation of CT perfusion maps for patients, a motion correction algorithm was developed to correct for patient breathing motion and evaluated against algorithms from commercially available CT perfusion software.

In a second step, in-house developed software was employed for a quantitative evaluation of DECT iodine maps against CT perfusion maps. To determine an optimum acquisition time for DECT iodine maps, they were mathematically assessed for their correlation to CT perfusion

maps of different perfusion parameters depending on their acquisition time. The resulting optimum acquisition time for DECT iodine maps of blood flow was validated by correlating DECT iodine maps acquired at peak tissue-enhancement to CT perfusion maps of blood flow in a second study. Finally, the use of bolus tracking was quantitatively investigated for the acquisition of DECT iodine maps of tissue perfusion. Additionally, DECT iodine maps were assessed for their potential to differentiate healthy pancreatic tissue and pancreatic carcinoma throughout all evaluations.

The achieved results show a high correlation between DECT iodine maps and CT perfusion maps of different parameters, depending on the acquisition time of the DECT series. Based on the quantitative evaluation, an acquisition window of DECT iodine maps using the acquisition technique of bolus tracking can be proposed between five to eleven seconds after contrast-enhanced arterial phase CT acquisitions routinely used in the abdomen. The results indicate that DECT iodine maps acquired using bolus tracking would show a high correlation to CT perfusion maps of blood flow and that measured iodine concentrations exhibit a statistically significant difference between healthy pancreatic tissue and carcinoma. While DECT iodine maps acquired at peak tissue-enhancement also show high correlation to CT perfusion measurements, they were outperformed by the results obtained for bolus tracking. Furthermore, the dose reduction potential compared to CT perfusion acquisitions at 80 kV_p was estimated to be up to 95%.

Contrast-enhanced CT acquisitions are routinely performed using bolus tracking, which is the standard of care for the examination of abdominal tumors. Therefore, the proposed acquisition of DECT iodine maps is easily integrated into current clinical workflows and could provide a quantitative and reproducible imaging biomarker for tissue perfusion at drastically reduced patient radiation exposure compared to "conventional" CT perfusion.

Potential applications of DECT iodine maps of tissue perfusion include the measurement of tumor angiogenesis, providing a direct assessment of tumor pathology. This information could be used for a more accurate tumor classification needed for the optimization of therapy planning or as an evaluation of the response to therapeutic intervention, allowing for individualized treatment using chemo- or radiotherapy.

Additionally, DECT post-processing could be used to gain even more information from the proposed DECT acquisition using bolus tracking. Virtual non-contrast images, approximating a baseline image without contrast agent, might be used to replace native phase acquisitions, providing additional dose reduction potential. Further applications of DECT material decomposition include the quantification of fat and iron, which could allow for more accurate personalized therapy planning. For example, fat and iron concentrations in the liver give information on liver pathologies, which is important for the estimation of functional liver volume for surgical resection.

In conclusion, the evaluation against CT perfusion maps shows promising results for the proposed acquisition of DECT iodine maps of tissue perfusion using bolus tracking. While further validation and a thorough analysis of diagnostic impact is required, the use of DECT iodine maps as a quantitative imaging biomarker for tissue perfusion shows great potential.