PhD Thesis Title: Functional, Volumetric, and Textural Analysis of Malignant Pleural Mesothelioma Using Computed Tomography and Deep Convolutional Neural Networks

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ABSTRACT:

Malignant pleural mesothelioma (mesothelioma) is a malignancy of the pleura, a membrane lining the outside of the lungs and the inside of the chest wall. This thoracic cancer is primarily caused by asbestos exposure and carries a poor prognosis. Computed tomography (CT) is the main imaging modality used for the diagnosis and treatment evaluation of mesothelioma in the United States. Mesothelioma is typically aspherical and has different morphology and growth patterns from most other cancers. These aspects of the disease, combined with recent advances in personalized therapies and molecularly targeted therapies, have motivated investigations into alternative and potentially more sensitive measures of mesothelioma treatment response. The image-based measurement of mesothelioma tumor volume has seen interest from researchers in the staging of this disease, and as a potential marker for patient prognosis and tumor response to treatment. The histologic subtype of mesothelioma is the most significant prognostic factor for this disease.

The first study presented in this work investigated the use of dynamic contrast-enhanced CT (DCE-CT) for the assessment of mesothelioma response to treatment. This prospective study showed differing trends in hemodynamic change between scans for patients on treatment and patients on observation. It suggests a potential role of this imaging method for the assessment of tumor response to treatment. A future study of a larger patient population on more coherent treatment regimens is needed to confirm the results of this pilot study. In another investigation of this work, deep convolutional neural networks (CNNs) were implemented for the automated segmentation of mesothelioma tumor on CT scans, which significantly improved the segmentation performance when compared with a previously published non-deep learning-based method for the automated segmentation of this disease. This study demonstrated the suitability and state-of-the-art performance of deep CNNs for the task of mesothelioma tumor segmentation on CT scans. Next, a study investigated the performance of a deep CNN-based tumor segmentation method on CT scans that exhibited both mesothelioma tumor and pleural effusions, a common presentation on radiologic scans of mesothelioma patients. This study showed significantly improved tumor segmentation performance when compared with the previous deep CNN-based method on scans of mesothelioma patients exhibiting tumor and pleural effusions. The last study presented in this work explored the differentiation of histologic subtypes of mesothelioma on CT scans using texture analysis through a retrospective investigation. CT scans of patients with pathologically confirmed epithelioid and non-epithelioid mesothelioma (i.e., biphasic and sarcomatoid tumors), acquired prior to talc pleurodesis, were included in the final analysis. The database of this study included in-house scans and outside scans acquired on a variety of CT scanners, and data heterogeneity precluded the robust classification of tumors as epithelioid and non-epithelioid; however, the method warrants further investigation as more data become available.

This dissertation investigated methods for the quantitative image-based analysis of mesothelioma tumor through standard contrast-enhanced and functional imaging and through the acquisition of image-based tumor volume using advanced deep learning-based algorithms. In this work, the novel investigation of deep CNNs for the segmentation of mesothelioma on CT scans demonstrated the state-of-the-art performance of

this technique for the automated acquisition of mesothelioma tumor volumetrics, the first pilot study dedicated to the investigation of DCE-CT for mesothelioma treatment response assessment indicated that this method should be explored in a larger patient cohort, and texture feature analysis was explored for the first time for the differentiation of mesothelioma tumor subtype in a retrospective study. The research presented in this work will hopefully advance the methods available to researchers and clinicians for the quantitative analysis of mesothelioma in the image-based management of mesothelioma patients.

References to author publications that relate specifically to the dissertation:

1. **Gudmundsson E,** Straus CM, Armato SG. Deep convolutional neural networks for the automated segmentation of malignant pleural mesothelioma on computed tomography scans. *J Med Imaging*. 2018;5(03):1. doi:10.1117/1.JMI.5.3.034503

2. **Gudmundsson E**, Labby Z, Straus CM, et al. Dynamic contrast-enhanced CT for the assessment of tumour response in malignant pleural mesothelioma: a pilot study. *Eur Radiol*. 2019;29(2):682-688. doi:10.1007/s00330-018-5533-9

3. **Gudmundsson E**, Straus CM, Li F, Armato SG. Deep learning-based segmentation of malignant pleural mesothelioma tumor on computed tomography scans: application to scans demonstrating pleural effusion. *J Med Imaging*. 2020;7(1). doi:10.1117/1.jmi.7.1.012705