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Diffusion MRI for tumor microstructure imaging using VERDICT modeling

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Blå stråket 5, den 13 juni, klockan 13:00

av Lukas Lundholm

Fakultetsopponent:
Henrik Lundell, Associate professor
Danmarks Tekniske Universitet, Danmark

Avhandlingen baseras på följande delarbeten

I. VERDICT MRI for radiation treatment response assessment in neuroendocrine tumors. Lundholm L, Montelius M, Jalnefjord O, Forssell-Aronsson E, Ljungberg M. NMR in Biomedicine, 2022; 35(6):e4680

II. Cluster analysis of VERDICT MRI for cancer tissue characterization in neuroendocrine tumors. Lundholm L, Montelius M, Jalnefjord O, Schoultz E, Forssell-Aronsson E, Ljungberg M. NMR in Biomedicine, 2025; 38 (6):e70050

III. A Monte Carlo-derived model of extracellular diffusion in solid tumors. Lundholm L, Montelius M, Jalnefjord O, Forssell-Aronsson E, Ljungberg M. Manuskript

IV. Effect of echo time on VERDICT MRI parameter estimation in brain tumors. Lundholm L, Jalnefjord O, Montelius M, Laesser M, Olsson Bontell T, Corell A, Jakola AS, Björkman-Burtscher I, Ljungberg M. Manuskript

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

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Diffusion MRI for tumor microstructure imaging using VERDICT modeling

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Abstract

VERDICT is a method which uses a mathematical model that provides estimates of microstructural tumor tissue parameters based on diffusion-weighted MRI data. It is a promising imaging method for non-invasive *in vivo* evaluation of whole-tumor tissue. However, model assumptions may introduce systematic errors in parameter estimates.

The aim of this thesis was to assess the use of VERDICT for tumor tissue evaluation and investigate the impact of model assumptions on parameter estimates, as well as to develop and evaluate methods addressing accuracy issues related to some of these assumptions.

The standard clinical approach for evaluating tumor treatment response is by measuring changes in gross tumor volume. However, such changes can be slow, and methods sensitive to microstructural changes may detect response earlier. Paper I investigates the use of VERDICT parameters for radiation treatment response assessment and shows that early parameter changes correlate with treatment outcome.

Histological analysis remains the gold standard for assessing tumor microstructure, but tumor heterogeneity limits biopsy representativeness. Paper II explores the use of VERDICT for whole-tumor tissue classification as a potential complement to histology. The work shows that multidimensional cluster analysis of VERDICT parameters enables classification of distinct tumor tissue types.

Model assumptions can introduce systematic errors in parameter estimates. Paper III investigates the effect of assumptions related to extracellular–extravascular diffusion and presents a Monte Carlo-based model which explicitly accounts for diffusion time dependence. Paper IV investigates the impact of including compartment-specific T2 relaxation in the model, in contrast to uniform T2 relaxation across compartments as assumed in conventional VERDICT. These works show that model assumptions can significantly influence parameter estimates and present methods to mitigate their effects.

In conclusion, the results of this thesis highlight the importance of accurate model assumptions in VERDICT, and demonstrate the model's potential for non-invasive, whole-tumor evaluation of tumor tissue in various applications.

Keywords: cancer, histology, Monte Carlo, radiation therapy, treatment response, clustering, biophysical modeling

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