BRACCO FELLOWSHIPS - EDUCATION IN RESEARCH

Project 8:

Machine learning with "Asphericity": A novel imaging biomarker for breast cancer with 18F-FDG PET/MRI

NAME OF INSTITUTION: Medical University of Vienna, Department of Biomedical Imaging and Image-guided Therapy, Division of Gender and Molecular Imaging, Vienna/AUSTRIA

RESEARCH GROUP AND ITS MISSION:

The main fields of research interest are clinical and experimental investigations on a cellular and sub-cellular level to diagnose cancer non-invasively and to monitor responsiveness to treatment. We focus on a more accurate cancer characterization through the synthesis of anatomical, functional, and molecular imaging information derived by different biomedical imaging methods. The working group of Prof. Helbich developed and optimized several imaging methods on the basis of MRI/PET, different molecular imaging tools, as well as minimal invasive diagnostic techniques particular in breast and prostate cancer.

BACKGROUND:

Tumour heterogeneity - both on a genetic and histopathological level - is a well-recognized feature of malignancy that reflects areas of high cell density, necrosis, haemorrhage, and myxoid changes and increased heterogeneity is associated with malignancy in general as well as more aggressive tumour subtypes (1) such as HER2 positive or triple negative breast cancer. However, it is difficult to fully and reliably assess intratumoral heterogeneity by biopsy as this invasive tissue sampling only provides snapshots and cannot comprehend tumour heterogeneity in its entirety.

Machine learning with "asphericity" of 18F-FDG PET/MRI, which is quantitative measure for spatial heterogeneity of the 18F-FDG uptake, has been introduced and shown promising results as a diagnostic and prognostic indicator in head & neck (2), lung cancer (3, 4) and prostate cancer (5) patients. To date his potential for the differentiation of benign and malignant breast tumours and different molecular breast cancer subtypes has not been explored.

HYPOTHESIS:

a) Proof of concept: We hypothesize that machine learning with asphericity of 18F-FDG PET /MRI, a quantitative measure for spatial heterogeneity of 18F-FDG uptake, can differentiate benign and malignant breast tumours.

b) Implementation in a multiparametric imaging concept: We hypothesize that machine learning with asphericity of 18F-FDG PET can be implemented in a multiparametric PET/MRI imaging concept and improves diagnostic accuracy of breast cancer diagnosis.

c) We hypothesize that machine learning with asphericity of 18F-FDG PET/MRI may lead to a better understanding of different molecular breast cancer subtypes.

OBJECTIVES:

- To evaluate whether asphericity with 18F-FDG PET can differentiate benign and malignant breast tumors and compare it to SUV metrics, metabolic tumor volume and total lesion glycolysis
- To compare the diagnostic accuracy for breast cancer diagnosis of multiparametric 18F-FDG PET/MRI using DCE, DWI and asphericity to single parametric DCE MRI and mpMRI with DCE MRI and DWI
- To investigate whether asphericity with 18F-FDG PET can differentiate different molecular breast cancer subtypes

APPLICANT'S DUTIES:

- Attend regular research meetings and journal clubs. Get familiar with the current literature
- Data processing, data storage and analyses of several already acquired multiparametric PET/MRI studies. Run statistic tests under
- Presentation of results, manuscript preparation and submission to a research journal. Supervision will be provided in all steps of the project by the PI and co-authors

APPLICANT'S BENEFITS:

- Understand the principle of multiparametric breast PET/MRI
- Use multiparametric breast PET /MRI in clinical practice

- This fellowship will educate participants in state-of-the-art breast imaging and further advance the implementation of mpPET/MRI of the breast in clinical
- In addition, the fellowship will lead to a wider understanding of clinical research and will lead to scientific presentations at international congresses and publications.

Project Leader: Prof. T. Helbich
Members: Prof. M. Hacker, Prof. P. Kapetas, Prof. P. Baltzer, Prof. A Haug

LITERATURE

1. Becker TE, Ellsworth RE, Deyarmin B, Patney HL, Jordan RM, Hooke JA, et al. The genomic heritage of lymph node metastases: implications for clinical management of patients with breast cancer. Ann Surg Oncol. 2008;15(4):1056-63.
2. Apostolova I, Steffen IG, Wedel F, Lougovski A, Marnitz S, Derlin T, et al. Asphericity of pretherapeutic tumour FDG uptake provides independent prognostic value in head-and-neck cancer. Eur Radiol. 2014;24(9):2077-87.
3. Hofheinz F, Lougovski A, Zophel K, Hentschel M, Steffen IG, Apostolova I, et al. Increased evidence for the prognostic value of primary tumor asphericity in pretherapeutic FDG PET for risk stratification in patients with head and neck cancer. Eur J Nucl Med Mol Imaging. 2015;42(3):429-37.
4. Apostolova I, Rogasch J, Buchert R, Wertzel H, Achenbach HJ, Schreiber J, et al. Quantitative assessment of the asphericity of pretherapeutic FDG uptake as an independent predictor of outcome in NSCLC. BMC cancer. 2014;14:896.
5. Meissner S, Janssen JC, Prasad V, Brenner W, Diederichs G, Hamm B, et al. Potential of asphericity as a novel diagnostic parameter in the evaluation of patients with 68Ga-PSMA-HBED-CC PET-positive prostate cancer lesions. EJNMMI research. 2017;7(1):85.

WORK PLAN:

Patients

In this IRB-approved prospective study a retrospective data analysis of 100 consecutive patients who underwent state-of-the-art mpPET/MRI of the breast with DCE-MRI, DWI and the radiotracer 18FFDG will be included. All patients fulfilled the following inclusion criteria: 18 years or older, not pregnant or breastfeeding, clinical or imaging abnormality mammography or breast ultrasound (BIRADS 4/5), no previous treatment, no contraindications to MR imaging or contrast agents. In all patients either histopathological verification of the lesion will be performed regardless of the results of 18F-FDG PET/MRI.

Image Analysis

Lesion localization, size, lesion morphology per BI-RADS and semi-quantitative enhancement kinetics with DCE-MRI, ADC metrics with DWI and asphericity, metabolic tumor volume and total lesion glycolysis with 18F-FDG PET will be recorded. In addition, breast parenchymal enhancement and amount of fibroglandular tissue will be noted. Examinations will be classified as either normal (no indication of malignancy) or abnormal (suspicious finding, further assessment necessary). A BI-RADS rating (1-5) will be assigned for each individual parameter as well as for multiparametric MRI and 18F-FDG PET/MRI.

Statistical Analysis

Appropriate statistical tests will be used to assess and compare sensitivities, specificities, and diagnostic accuracies in Objectives 1/2/3. Histopathology will be used as the standard of reference. In breast cancer cases, molecular breast cancer subtypes will be derived via immunhistochemical surrogates: luminal A if either ER or PR was positive and HER2 was negative, Luminal B if either ER or PR was positive and HER2 positive, HER2-enriched if ER and PR were negative and HER2 positive and basal-like if ER, PR and HER2 were negative.