Department of Molecular Medicine and Surgery

Computed Tomography Based Assessment of Treatment Response in Solid Tumors

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av

Chikako Suzuki
M.D.

Huvudhandledare:
Professor Lennart Blomqvist
Department of Diagnostic Radiology
Department of Molecular Medicine and Surgery
Karolinska Institute, Stockholm, Sweden

Bihandledare:
Professor Hans Jacobsson
Department of Nuclear Medicine
Department of Molecular Medicine and Surgery
Karolinska Institute, Stockholm, Sweden

Dr. Hirofumi Fujii
Functional Imaging Division
Research Center for Innovative Oncology
National Cancer Hospital East, Kashiwa, Japan

Fakultetsopponent:
Professor Katrine Åhlström Riklund
Umeå Centre for Functional Brain Imaging
Umeå University, Umeå, Sweden

Betygsnämnd:
Docent Per Liss
Department of Radiology, Oncology and Radiation Science, Radiology
Uppsala University, Uppsala, Sweden

Professor Nils Albiin
Department of Clinical Science, Intervention and Technology (CLINTEC)
Karolinska Institute, Stockholm, Sweden

Docent Michael Bergqvist
Department of Radiology, Oncology and Radiation Science, Oncology
Uppsala University, Uppsala, Sweden

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ABSTRACT

A “substantial evidence” of effectiveness is required for new cancer treatment regimens to be approved. Objective tumor shrinkage/enlargement has been adopted as an indicator of drugs efficacy. The change of tumor size is assessed and quantified by various radiological techniques; most commonly computed tomography (CT). A high accuracy and reproducibility is, for obvious reasons, necessary in order to achieve a meaningful evaluation of such studies. For that purpose, the World Health Organization criteria (WHO-criteria) were launched in 1979 followed by the Response Evaluation Criteria In Solid Tumors (RECIST) in 2000 and the updated version RECIST 1.1 in 2009. There are, however, still several steps that may deteriorate consistencies.

The purpose of this thesis was to investigate causes that may affect inconsistency in evaluation procedure according to RECIST (study I and II) and to explore the percentage of tumor size change at the first follow-up CT as the potential new surrogate indicators for OS in patient with metastatic colorectal cancer (mCRC) (study III) and in patient with metastatic breast cancer (MBC) (study IV).

The number of discordant cases increased gradually when assessing fewer target lesions. Measuring fewer than four target lesions might cause discrepancies when more than five target lesions were present (study I). Interobserver variation using RECIST and WHO-criteria were moderate: 0.53 (95%CI 0.33 - 0.72) and 0.60 (0.39 – 0.80), respectively. Intraobserver variation using RECIST and WHO-criteria were substantial to perfect that ranged between 0.76 – 0.96 and 0.86 – 0.91, respectively (study II).

The initial change in tumor size 8 weeks after initiation of chemotherapy was prognostic for PFS: Hazard Ratio (HR) 2.21, 95%CI 1.97 – 2.49, and OS: HR2.01, 95%CI 1.75 – 2.31, in mCRC (study III). The initial change in tumor size also correlated with OS in MBC (study IV). A marked difference in OS between patients with or without new lesion was demonstrated in mCRC: HR 3.77, 95%CI 2.08 – 6.83 (study III) and in MBC: HR 4.29, 95%CI 2.44 – 7.53 (study IV).

In conclusion, the current tumor response evaluation criteria are associated with several subjective steps that may cause inconsistent results. The initial change in tumor size at the first follow-up CT may provide an alternative surrogate outcome. The findings obtained in this thesis may improve the development of future response evaluation criteria.

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