Postprocessing and Cross Validation

Modeling and Quantification

Modelling Applications in Oncology Studies

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Learning Objectives:

- Understand the need for quantification in response monitoring
- Understand the difference between semi-quantitative and fully quantitative approaches
- Obtain an overview of modelling in oncological studies

The two most important characteristics of PET are its quantitative nature and its high sensitivity. In oncology, its sensitivity has been used successfully, in particular for detecting (distant) metastases using [^{18}F]FDG. . This has led to a significant improvement in staging with direct consequences for selecting the most appropriate therapy. It is clear that, for detecting metastases, quantification is not needed, as one only needs to find out whether they are present.

Based on its success in staging, PET increasingly is used to monitor response to therapy. In fact, [^{18}F]FDG PET already is used as a surrogate endpoint in the development of new anticancer drugs. Clearly, visual assessment of response scans has limited value, as it can only be used in extreme cases. Quantification is needed for evaluating more subtle changes. In addition, it is needed to define objective cut-off points for multi-centre trials. Finally, visual assessment makes the inherent assumption that normal tissue (i.e. background) is unaffected by the therapy. This assumption may not be correct and is not needed in quantitative assessments.

The majority of [^{18}F]FDG PET response studies have been analysed using the Standardised Uptake Value (SUV), which represent uptake in a tumour normalised to injected dose and body weight (normalisations to body surface area and lean body mass have also been used). The advantage of SUV is that it combines a static (whole body) scanning protocol with a simple way of analysing the data. It is, however, sensitive to various patient and protocol related factors. Consequently, significant efforts have gone into harmonizing acquired data with guidelines formulated by, for example, EORTC, NCI and EANM.

There is no doubt that, for many therapies, measured [^{18}F]FDG SUV changes provide valuable information on the response (early) during therapy. Nevertheless, SUV represents a measurement at a single time point (after injection) and it assumes that [^{18}F]FDG availability is predictable, i.e. (after normalisation) is the same from patient to patient and from baseline to response scan. With novel therapies this is not necessarily the case. For example, if a therapy results in an inflammatory response in other parts of the body, there will be increased [^{18}F]FDG uptake in those inflammatory tissues, leading to faster clearance from plasma. This, in turn, will lead to lower net delivery to the tumour and the relationship between SUV and the real parameter, glucose metabolism, will be change. Consequently, in those cases, misleading information will be obtained when comparing SUV before and after therapy, and proper results can only be obtained by full kinetic analyses of dynamic PET data.

Another application of tracer kinetic modelling in oncology is the prediction of response to anticancer therapy. In this case the anticancer drug itself is labelled and tracer amounts are injected prior to any therapy. Tumour rate constants are derived from such a tracer study and, combining those rate constants with the plasma profile during therapy, may provide a means to predict whether tumour concentrations of (cold) drug will be high enough for a therapeutic effect.