A systems model for cancer clinical trial imaging

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Description:

A new drug in Oncology is routinely assessed using imaging via the Response Evaluation Criteria In Solid Tumours (RECIST) (1,2). Within the metastatic setting RECIST requires that a patients' tumours are categorised into "target" and "non-target" lesions. The choice of whether a lesion is a target or non-target lesion is predominantly based on size and ease of measurement. The target lesions are recorded quantitatively over time through measurement of their longest diameter whereas the non-target lesions are recorded qualitatively over time. Non-target lesions are placed in one of 3 categories at each time-point: no-change/partial response, complete response or unequivocal growth (progressive disease). Measurement of target and non-target lesions continues until the disease progresses: 1) the sum of longest diameters of the target lesions increases by 20% over the minimum recorded; or 2) non-target lesion unequivocally progresses; or 3) a new lesion is observed; or 4) the patient dies. The reason for progression is usually reasons 1,2 or 3. At the point of disease progression the current treatment is stopped and no more imaging data is collected and the patient is considered to be in the follow-up phase of the study.

There has been a considerable amount of modelling work done on analysis of the target lesions mainly using the sum of longest diameters with the bulk of it focussed on coming up with correlates to survival (3,4) – with dubious success (5,6). The aim of this project is to not look for yet another correlate to survival but to explore the connectedness of the disease across the multiple sites within a patient. That is generate models/analysis methods to explore the correlation patterns between the imaging variables recorded and assess if these are different across treatment types. The resultant model/analysis method is likely to improve our understanding of the clinical disease but will also advance the type of PKPD data analyses that can be conducted.

Data Provided:

Routinely collected imaging time-series data from phase III clinical trials within non-small-cell lung cancer will be provided. The therapies will be paclitaxel/carboplatin combination, docetaxel and erlotinib (1st generation EGFR inhibitor). The time-series imaging data will consist of longest diameters of target lesions, qualitative descriptions of non-target lesions and all information on when and if new lesions occur.

No sub-cellular information (e.g. genotype or pathway level markers) is available on the lesions. Thus it is envisaged a multi-scale model is not likely to be required.

Questions of interest:

1) Is there a correlation between the different imaging variables over time?
2) Can the observations on one type of imaging variable at time *t* be used to predict what will happen to another imaging variable at time *t+1*?

References:

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