

The monitoring of tumour response to treatment.

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This is one of the current challenges to Nuclear Medicine. Can it deliver a quantitative answer to response assessment that is better based, more reliable and easier to apply to single or serial studies of cancer image data than its radiological counterparts? From basic principles it should be able to do so, as cancer is a biological entity and a biological response should antedate physical change.

The X-ray CT RECIST criteria rely on the largest diameter of the mass and its change with treatment a 30% decrease is taken as a Partial Response (PR), a 20% increase as Progressive Disease (PD). Stable Disease (SD) is a change less than the above and Complete Remission (CR) is disappearance of the tumour mass. RECIST has been criticised widely as time consuming it has to be applied to e.g. all ten liver metastases. It depends on a well defined tumour edge physically which may not be the biological edge of the tumour. It seems inconsistent with biological reality to use a single diameter when tumour volume, which is readily available from CT, is likely to be and has been shown to be a much more sensitive index of response.

Nuclear medicine's assessments are based on a visual or measured reduction of uptake by the tumour as an index of response. Is it reliable? The visual response depends on the reproducibility of administered dose, examination time and conditions and the display characteristics. The problem is compounded by the likely down-regulation of the receptors for peptide studies and the inability of FDG to distinguish between dormancy and death. 'Sick cells don't eat'. A therapy induced inflammatory response will enhance FDG uptake giving apparent progression when the biological response is in fact favourable. The time chosen to assess the response e.g. the day before the second cycle of chemotherapy appears to vary according to tumour type.

Nuclear medicine claims it is quantitative or at least semi-quantitative so a measure of uptake is able to show the change between two studies. The problems of SUV for PET are well documented. The basic one is a lack of a rigorous way of defining a region of interest. Should that used for the first study be transported to the second study what if as is hoped the tumour has shrunk? Should the threshold e.g.

37% for the first study be used for the second or should the peak value or peak plus its neighbouring eight pixels/voxels? Perhaps the way ahead is to combine by software image fusion the volume change from CT with the measurement change from receptor scintigraphy or PET. Who then will undertake and how is a validation trial to be set up? Who will support it? Is the IAEA or the NCI able to do so? As usual answers pose more questions. Nevertheless there is progress and progress still to be made. The drug companies are looking for validated imaging support to give surrogate end points to reduce the number of patients required, simplify the protocols and reduce their expense. Even the FDA is beginning to recognise the potential of serial image data as a measure of therapeutic response. It is up to the Nuclear Medicine community to find and validate better solutions.

Keith E. Britton