Problems in the assessment of treatment response

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In this review reasons for difficulty with assessment of treatment response are discussed and general principles for reducing these problems are advanced. Discussion focuses on: (1) adoption of common examination protocols; (2) use of structured reporting of examinations; and (3) the value of multidisciplinary meetings for resolution of uncertainty.

Assessment of treatment response involves comparison with a previous examination. Thus reproducibility between serial examinations is vital. Reproducibility is most likely when the same imaging test is used for serial examinations and is performed in a similar manner. In the context of clinical trials and research studies operator-independent tests such as computed tomography (CT) are preferred to ultrasound and increasingly CT is used in routine clinical practice. Even using CT there is considerable scope for variation in performance: enhanced vs. unenhanced; differing contrast techniques; spiral vs. non-spiral. Key to minimizing variation is the adoption of common protocols.

The need for reproducibility is emphasized when patients change institutions, e.g. when referred from a cancer unit to a cancer centre, or vice versa in shared care. The evidence from a recent audit of standards of cross-sectional imaging conducted within the North West of England[1] was that performance in body CT was of high quality and that central review of imaging resulted in a change in treatment for only 4% of patients[1]. However, the hard copy transferred was incomplete in one in three cases and the calibration rule was absent in one in 10. The first deficiency reflects poorly upon file-keeping. Proponents of PACS and image transfer will argue that such obstacles can be surmounted but thus far image transfer at inter-hospital level has been tested widely only in the context of emergency neuroradiology. Inclusion of a calibration rule is a basic requirement and this should be standardized easily.

Modern cancer care must include shared imaging protocols and shared copy of these examinations. This works best in an environment of discussion, education and research. Network groups are developing for individual cancers and clinical specialties and the North West of England has a well-developed centre-led forum for unit–centre discussion of imaging protocols. The recent capital replacement programme for CT makes it more likely that most cancer units can achieve rather than simply aspire to cancer centre protocols and standards. The Royal College of Radiologists (RCR) guidelines for the use of CT imaging[2] are now almost a decade old but still provide valuable information and define a minimum standard for CT examinations which should now be universally achievable. The document also includes a few suggestions as to how the findings of CT examinations should be reported.

A common difficulty in routine practice is non-availability of the previous (comparator) study, whether performed in-house or at St Elsewhere's. However, a report of that examination which clearly records information on its technique and findings will allow a reproducible study to be performed and a focused comparison with recorded marker lesions. A structured report for such studies improves agreement and understanding between radiologists. It also provides clarity and consistency for clinical colleagues.

Reporting styles vary but use of a framework and inclusion of a certain key features within the report is suggested. It is helpful to comment on the clinical context of and indication for the examination and to record the diagnosis and reported clinical stage, e.g. newly diagnosed cancer of cervix, clinically T1b. A record of this in the imaging history can be valuable when follow-up requests omit such detail. Further, this detail indicates the context in which the radiologist formed his or her assessment. A brief note of the technique, to ensure consistency in subsequent examinations, should also note any complications or patient preferences regarding oral or intravenous contrast. Cancer patients are frequent and discriminating consumers! Description of the key findings should be in sufficient detail for identification of important (marker) lesions by colleagues by indicating the anatomic site (lobe or segment), bidimensional measurements and the table position/slice number at which this assessment was made. Only a third of examinations in the North West audit included such data[1]. When comparison is made with previous studies this should indicate with which study and its date. Finally, wherever possible a conclusion or impression should, for initial staging or relapse assessment studies, record tumour stage and bulk using either the TNM system or the predominantly used clinical staging scheme and where possible a judgement regarding treatment options (e.g. suitability for radical local therapy). For treatment response examinations the impression should categorize this as partial or complete response, stable or progressive disease.

Finally, how are uncertainties and problems resolved? Second review of imaging is widely practised in cancer care and expert review proves valuable for a significant minority of patients. Most work has looked at initial staging examinations rather than in treatment response assessment. The higher proportion of changed diagnoses

and management plans after expert review in North American studies[3–5] than in UK series[1] likely reflects greater variation in practice standards in the USA. Review work should ideally occur within the context of a multidisciplinary team (MDT) meeting. Such work is time-consuming and requires the attendance of key radiologists, pathologists, surgeons, physicians and paramedical staff, as well as the support of administrators and clerical staff. Notes, films and slides must all be available and in this forum clinical and pathological information is often brought to light which resolves problems, downgrades the clinical impact of radiological uncertainty or else discussion helps to form management or investigation plans to respond to this. There is little reported research on the value of such meetings but such as it is the data are clear. Clinicians place high value on time spent within such meetings and they are time-effective for radiologists[6,7].

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Ovarian cancer — difficulties in monitoring response

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The imaging of malignant disease involves tumour diagnosis, staging, measurement of response and identification of complications. Increasingly, oncologic radiologists are expected to provide objective assessment of change in masses, on serial studies, in order to validate response or resistance to new chemotherapeutic agents. In some cancer centres follow-up examinations make up over 75% of computed tomography (CT) activity.

Objective assessment on CT depends on a somewhat simplistic assumption that those masses that increase in size define disease progression, whereas reduction in tumour size indicates a favourable therapeutic impact. The 1979 WHO Handbook and the 1981 paper by Miller *et al*.[1] identified criteria for bi-dimensional measurements of tumour masses and established the classification of Complete Response (CR), Partial Response (PR), Stable Disease (SD) and Progressive Disease (PD). It has became apparent, however, during the application of these criteria that assessments based on bi-dimensional measurements of one or two marker lesions could result in misleading conclusions, particularly in respect of progressive disease where increasing size of a single lesion might be at variance with favourable change elsewhere. This could lead to an incorrect conclusion that therapy was ineffective. It has also become clear that methods for evaluating change in the size of measurable lesions have not always been universally applied and different observers and even centres could employ different regimes. Husband, Gwyther and Rankin highlighted these features in 1999[2] when they described the problems of bi-dimensional measurements of 3-dimensional masses, as well as the difficulties posed by tumour necrosis and calcification.

In June 1999 a revised version of WHO criteria under the heading 'Response Evaluation Criteria in Solid Tumours (RECIST criteria)'[3] was published, based on the assessment of up to 10 target lesions, the sum of whose longest diameters define the baseline measurement. The stimulus for this finite objective measurement emanates from the licensing authorities, whose requirements define phase II drug assessment protocols for the pharmaceutical industry. RECIST criteria require the identification up to 10 solid, well-marginated nodules and their repeated identification and assessment of