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Short communication

Late effects of radiotherapy: how to assess and improve outcomes

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The British Institute of Radiology was the venue in May 2004 for an excellent conference addressing issues regarding the recording and analysis of late effects of radiotherapy treatments. Currently there is increasing interest in radiotherapy dose escalation using conformal treatments and novel therapies such as intensity-modulated radiotherapy. In view of the steep dose–response relationship with radiotherapy, dose escalation can be dangerous unless undertaken carefully with accurate reporting of late serious adverse effects, so that the therapeutic ratio of treatments can be determined. The meeting attempted to address issues around assessment of treatment outcomes with a view to consensus regarding current and future practice.

Professor Anne Barrett outlined some of the work in this area achieved by the Recording, Education and Amelioration of the Consequences of Treatment group (REACT). REACT was set up under the auspices of the European ESQUIRE Project [1]. ESQUIRE is co-ordinated by the European Society for Therapeutic Radiology and Oncology with the objective of improving treatment outcomes for cancer patients by addressing various facets of radiotherapy implementation and training. Currently there are a variety of systems in place for the recording of late effects of treatment, including from the RTOG/EORTC, NCI-CTC3 (Common Toxicity Criteria) and the Anglo-Franco system, in addition to inhouse non-validated approaches. Professor Barrett also presented results of an audit undertaken of follow-up practice in Europe. Four centres in the UK were involved in this study. In over 50% of visits patients and doctors reported disease or treatment related problems. There was an attribution bias in patients who, compared with doctors, were more likely to consider their problems related to disease than treatment. The use of a short scale to assess late morbidity of treatment, developed by Professors Dische and Saunders (Table 1), increased the recording of side effects from 23% before the study, to 90% [2]. Grade 3 or 4 late morbidity was reported to be in the range of 4–9%.

Detailed recording of late effects is difficult, given the complexity and time pressures existing in clinics. The LENT SOMA system is one of the most common systems for recording late effects [3]. It is recognized as being an extremely useful tool, as it includes both subjective as well as objective scoring measures, but is cumbersome and difficult to use in daily practice. Dr Susan Davidson from the Christie Hospital, Manchester, discussed their experience of the use of the LENT SOMA system for analysing late effects of radiotherapy treatment. There remain problems in defining what "acceptable toxicity" is, and this varies depending on whether it is a medical or patient view. Validated systems for assessing late effects need to be sensitive, reproducible, feasible and convenient. Although the LENT SOMA system has many of these features, it still could be improved further. The Christie Hospital has developed patient questionnaires based on the LENT SOMA for certain tumour sites, and suggest these could be developed into more useful tools. Details of these questionnaires can be found at: www.christie.nhs.uk/proinfo/departments/clinical_oncology/lent_soma.htm

What was clear is that the use of different reporting systems across the UK, Europe and worldwide makes cross comparisons of differing treatments difficult. This lack of a standardized approach was a theme throughout the conference, as was the need to simplify data collection and educate regarding the importance of recording late effects.

Dr Catharine West, from the Christie Hospital, tried to address the question of whether it is possible to predict normal tissue effects of radiotherapy in advance of treatment. She provided an excellent historical overview of the development of radiobiology understanding through the 20th century to the modern day. Recent developments make the possibility of predictive assays tangible, although as yet not practicable. In the post genomic

Table 1. Influence of the adverse effects due to cancer treatment upon the patient's life: a simple recording system [2]

0	No effect that can be related to cancer treatment or an effect so mild that it requires no regular medication or other healthcare intervention and does not interfere with normal life
1	Mild effects related to cancer treatment that are entirely or almost entirely controlled by medicine and/or other healthcare intervention and do not lead to anything more that a minor alteration in lifestyle
2	Moderate adverse effects related to cancer treatment, that requires continued use of medicine and/or health care intervention. The patient remains able to lead an independent existence although some modifications in activity and in style of living are necessary
3	Severe adverse effects. The patient's life is considerably affected by the adverse effects related to cancer treatment with a considerable and continued restriction of activities. Inpatient care and major surgery may have been required

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era, the concept of radiosensitivity is changing. Rather than mutations in a few DNA damage recognition and repair genes being responsible for intrinsic radiosensitivity, it is recognized that single gene inherent variation has more of a role to play (single nucleotide pleomorphisms). Identifying these variations and their implications on treatment related morbidity depends critically on the presence of a universally accepted tool for recording these late effects.

Sara Faithfull, from the European Institute of Health and Medical Sciences, and Dr Jane Maher from Mount Vernon Hospital, reflected on the current state of follow-up practice in the UK and the future challenges of developing patient care pathways. Different institutions have varying strategies with no consensus as to best practice. Follow-up places a large burden on limited resources. With growing cohorts of long-term surviving cancer patients, this burden is increasing. There are several traditional ''medical'' aims of follow-up. Specifically we aim to detect tumour recurrence early, assess effectiveness of treatment and record late morbidity of a treatment regimen. Patient expectations of follow-up can differ. They wish to define what is ''normal'' following treatment, to manage chronic health problems, to deal with psychosocial issues and social consequences of diagnosis and treatment. There are problems with our current practice and we need to consider service redesign and innovative strategies to encompass the aims of follow-up in the challenging new consumer driven environment. Nurse or radiographer led follow-up may be one of these approaches. Future follow-up may rely more on patient self-assessment and reporting of symptoms, with less emphasis on ''routine'' investigations. Particularly as there is little consensus or evidence as to which tests to do when, except in a minority of tumour sites. Technology, such as using the Internet for patient self reporting, may become routine. New care pathways need also to be seen in a different context. With an ageing population, and increased cancer survival, follow-up will not simply be about assessing the impact of radiotherapy treatments, but dealing with complex medical problems. ''Chronically ill people have multiple diagnoses, none of which are particularly revealing about the aggregate severity of illness'' (Lyn, 2003). Traditional models of follow-up will have to change.

Dr Jervoise Andreyev from Chelsea and Westminster Hospital and Imperial College, highlighted the importance of multidisciplinary approaches to the management of late effects, from the perspective of a gastroenterologist with specialist interest in this area. The most common symptoms precipitating referral for further investigation are rectal bleeding, urgency and frequency, and tenesmus causing significant problems impacting on quality of life. Faecal incontinence or leakage is a common symptom, frequently under-reported by patients and rarely an indication from clinicians for referral. Current late effect symptom measures are poor in assessing this particular side effect. While often these symptoms are automatically assumed to be due to prior radiotherapy, there is frequently another unrelated diagnosis, which may be amenable to treatment. In his personal experience of managing 257 patients, 12% had underlying neoplasia on further investigation, either disease recurrence or a new secondary tumour. Another diagnosis was made in 38% of patients. There may be simple measures that can be undertaken which may provide symptomatic relief. The input of specialists with in interest in the management of the late effects of radiotherapy will facilitate the development of new treatments, for example, in the management of faecal incontinence.

Professor Andrew Trotti, from the H Lee Moffitt Cancer Centre, USA, gave us a view of the recording and analysis of late effects from an American perspective. He has been in involved in the development of the National Cancer Institutes' Common Toxicity Criteria for grading side effects. The evolution of the multiplicity of grading systems was outlined culminating in the latest NCI common toxicity criteria system version 3 [4]. This latest version is the most comprehensive grading system to date, with 570 items, covering both acute and late effects. These systems generate plentiful data, but several issues arise with respect to further processing of this information. There are computer software systems in development to facilitate data collection. Even once the data are collected, the methodology of data presentation to allow cross comparison of treatments still has to be clarified. As we have CONSORT guidelines for reporting of studies, the aim is to develop similar standards for the reporting of late effects. The Adverse Events in Radiation Oncology Group (AERO) is one group attempting to address this issue. Another initiative is to develop a method for classifying treatment risks, analogous to the UICC TNM classification system used for tumour staging. ''TAME'' would aim to reflect aggregate risk of treatment by defining T, acute toxicity; A, adverse late effects; M, mortality; and E, end results. This information would help to standardize discussion with patients regarding treatment risk and benefit. It will be interesting to see how this initiative develops.

Ultimately there is further need for international consensus as to the best methods of data collection, which should be validated, sensitive, reproducible and user friendly. While the consensus is being defined, it is still essential we continue to collect data on late effects to assess the therapeutic ratio of our treatments. The Dische and Saunders short scale for toxicity assessment may be a useful initial tool for routine clinic follow-up given the current burdens on time and resources [2]. The LENT SOMA system is a comprehensive system and provides much information, but is difficult to implement in routine practice outside of clinical studies. Information technology certainly will facilitate future data collection, but there are cost implications of new software development and implementation. It is important to continue to push for co-ordinated approaches to late toxicity data collection at a National and International Level. The National Cancer Research Network is one of the forums to take these issues further. Patient care pathways will also need to develop and change in the context of an ageing population and increased numbers of patients on ''follow-up''. Novel strategies will be required for the recording of toxicity data as the ''traditional'' mode of follow-up changes. Projects such as REACT are aiming to develop international consensus on the recording and of reporting radiotherapy treatment outcome and will hopefully help to clarify these issues further.

References

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