Tailoring breast cancer therapy to genetic status

The conservative management of breast cancer with wide local excision followed by radiation therapy has been proven to be of equivalent efficacy to mastectomy for patients with stage I/II disease, and has been accepted as the standard of care for most patients with early-stage breast cancer.1,2 On the contrary, the appropriateness of breast-conserving therapy in carriers of a deleterious BRCA1/BRCA2 mutation is still a matter of debate, in view of the possible increased risk of an ipsilateral recurrence (either a true recurrence or a new primary breast cancer). Furthermore, there are concerns about the presumed damage of radiation on DNA in carriers of the BRCA1/BRCA2 mutation. Recently, Mark Robson and co-workers further explored the former issue and put this in perspective.3

The risk of radiation-associated side-effects in mutation carriers is not well studied. The only report investigating this issue in BRCA1/BRCA2 mutation carriers compared with sporadic controls was reported by Pierce et al.4 They found no differences in the rates of acute or chronic complications after a 5-year median follow-up.

Several authors, including our group, investigated the occurrence of ipsilateral and contralateral breast events after breast-conserving therapy in BRCA mutation carriers.5–7 While the risk of a contralateral breast cancer is uniformly high in all studies, whether family-based or population-based, results for ipsilateral recurrence are more disparate. One of the reasons for this inconsistency might be the difficulty in distinguishing a true recurrence from a second primary tumour in the same breast. Ways to disentangle these two entities are, for instance, to compare morphological and histochemical characteristics, to examine the location within the breast of the two events, and to consider the time elapsed since the primary tumour. Generally, recurrences that are (according to these criteria) more likely to represent a second primary tumour in the same breast appear more often in BRCA1/BRCA2 mutation carriers, whereas the risk of a relapse of the first tumour appears not to be higher than expected, probably by the protective effect of the radiation therapy.

Robson and co-workers provide additional data on the rates of ipsilateral and contralateral breast cancer after breast-conserving therapy in 87 patients identified as BRCA1 or BRCA2 mutation carriers at one institution. Their conclusions, with a median follow-up of 76 months, agree with most of the previous reports, confirming the high risk of contralateral breast cancer, whereas the overall risk of an ipsilateral recurrence appeared similar to those of young women with sporadic breast cancer, with 5-year and 10-year probabilities of 11.2% and 13.6%, respectively.

A drawback of Robson and co-workers’ study is that no comparisons were made with an internal control group but only with published data. Furthermore, it might have been interesting to present subgroup analyses excluding the small group of BRCA2 mutation carriers, as tumours associated with BRCA1 and BRCA2 clearly constitute different entities.8

The issue of ascertainment/longevity bias is recognised and discussed by Robson and co-workers. This problem is well-known in this type of study, in patients that have to be alive at the moment of DNA testing. The time between the date of initial diagnosis of breast cancer and the DNA result is described by Robson. For the risk of a contralateral breast cancer, Robson presents separate analyses for women with a breast cancer diagnosis less and more than 2 years before the DNA diagnosis, showing no significant difference between the subgroups in 5-year risk of a contralateral breast cancer. However, these subgroup analyses were not done for the other endpoint, local recurrence risk, although Robson does present data showing that the interval between breast cancer and DNA diagnosis was significantly longer in women with a local recurrence than in those without. The reason for this inconsistency is unclear.

Robson and co-workers’ paper presents a detailed overview of other published studies on the subject.
The National Service Framework: paediatric emergency care

Annually, children account for 3.4 million attendances to accident and emergency departments in the UK. Some of these attendances are a diagnostic and management challenge, because distinguishing trivial from serious illness can be difficult and children’s health can deteriorate quickly. Their best possible care depends on the provision of health services that deliver timely high-quality assessment, diagnosis, and treatment. The new National Service Framework (NSF), Standard 6—Children and Young People Who Are Ill provides guidance to primary-care trusts and commissioners about the provision of these services and should be welcomed by all involved in the care of children.

The keystones of the NSF are: the development of managed clinical networks; the practice of evidence-based care, maintained by clinical governance; improved availability of advice and support to parents and carers; ensuring there is a workforce of adequately trained and competent staff; and the sharing of information among health-care professionals.

Local emergency-care networks, involving providers of acute health care, will ensure that children are managed by agreed protocols for common and serious illnesses, allowing treatment to be contiguous across the network—ie, throughout tertiary, secondary, and primary care. Auditing the use of these protocols will ensure they are followed, and will allow them to be adapted according to local resources and requirements.

Information will be provided to children and parents on discharge about the condition being treated, with the pathways of care within the network delineated so that they can be followed by carers if the child deteriorates. Named individuals will be responsible for ensuring coordinated care is available in each locality, and ensuring that high-quality care is delivered.

The NSF states that all areas providing care to undifferentiated illness in children must be staffed by people competent and trained in paediatric assessment, and that staff of sufficient seniority are available to make decisions about appropriate investigation and management, alongside facilities for the observation and reassessment of children. Training of staff involved in the care of children is another important keystone of the NSF; it also recognises that health professionals

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We declare that we have no conflict of interest.


Although numbers generally are small, study designs differ, and the exact risk estimates are quite variable, the overall picture is that of a similar local recurrence rate in the short-term (<5 years), compared with age-matched sporadic cases, but an increased risk thereafter (>5–10 years).

We therefore agree with Robson and co-workers’ conclusions that the current indications for unilateral mastectomy in BRCA1/BRCA2 mutation carriers can be the same as for women with sporadic breast cancer. For the prevention of a second breast cancer (contralateral as well as ipsilateral), a bilateral mastectomy might be considered, but in selected cases.9 However, in the interest of the best care for the patient, we call for a multicentre and probably national or international approach to further study this subject in a multivariate design, with large and more homogeneous subgroups.

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