Received: 20 September 2021 | Revised: 15 December 2021 | Accepted: 28 March 2022

DOI: 10.1111/ecc.13584

COMMENTARY

European Journal of Cancer Care WILEY

Genomic sequencing in oncology: Considerations for integration in routine cancer care

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KEYWORDS: clinical practice, genome sequencing, genomic medicine, oncology, routine care

1 | INTRODUCTION

In the United Kingdom (UK), efforts to incorporate genome sequencing into clinical care were significantly boosted by implementation of the 100,000 Genomes Project in 2014. The UK now transitions to the next phase of delivering genomic sequencing within the National Health Service (NHS) via the Genomic Medicine Service (GMS). A National Genomic Test Directory has been developed to specify the genomic tests that can be ordered and funded by the NHS, including testing criteria, scope and technology. Mainstreaming of genomic sequencing is a key component of the GMS which enables multispecialty clinicians, including oncologists, to directly order specific genomic tests aimed at improving access to testing for their patients.

In practice, how genomic sequencing will be adopted and used within oncology remains unclear. A systematic review of factors for successful implementation of genomic medicine in routine health care identified the need for practice reform, genomics education and training, validation of clinical utility and cost-effectiveness, and adaptations to models of care (Pearce et al., 2019). In particular, the integration of genomics into mainstream oncology will require '… upskilling other healthcare professionals in genomics' to manage genomic testing capacity, interpretation of results and implementation of changes in clinical care (Bancroft et al., 2020). Healthcare professionals' views on the implementation of genomic sequencing into NHS clinical practice reported several concerns including lack of preparedness of non-genetics clinicians (Sanderson et al., 2019).

This commentary reflects on some of the factors to consider for integrating genomic sequencing in oncology and how they may impact the roles of the health professionals involved.

2 | CLINICIAN UPTAKE OF GENOMIC SEQUENCING

Whilst integration of genomics into standard NHS care will be transformational, practice of genomic genomic medicine and optimal utilisation of genomic information needs to be established in oncology. Factors such as perceived utility and confidence influence the uptake of genomic medicine by non-genetics specialists (Crellin et al., 2019). As noted, 'Their [clinicians'] perception of the utility of genomic testing, then, will be an important determinant of whether

[Correction added on 27 April, after first online publication: The first name of the sixth author was corrected in this version.]

it sees widespread uptake into clinical medicine' (Raghavan & Vassy, 2014). There may be uncertainty amongst clinicians as to the role of genomic medicine in improving patient care beyond current clinical practice (Crellin et al., 2019; Zebrowski et al., 2019).

The lack of clear treatment guidelines for somatic testing and referral guidance for germline testing has been seen as barriers to uptake (Vetsch et al., 2019). For some cancer types, there is proven clinical utility of genomic medicine; a persuasive example of this has been the recent development and licencing of PARP-inhibitors for somatic or germline mutated high grade serous ovarian cancer. Whilst there are other promising advances, currently genomic sequencing identifies a minority of patients with actionable genetic alterations where corresponding targeted therapies are available and approved for use in their specific condition (Berger & Mardis, 2018). In part, this is due to the lack of treatments that are available for use beyond their labelled indication, leading to a reliance on clinical trials or expanded access programmes; currently, it may be difficult to access drugs outside of their licenced indications regardless of the mode of action of the drug.

3 | GENOMICS KNOWLEDGE AND CONFIDENCE

There is a growing body of literature around oncologists' genomics knowledge and confidence. Oncology clinicians report some confidence regarding genomics; however, nearly a quarter indicated lack of confidence in their knowledge of genomics and ability to make treatment recommendations based on genomic data (Gray et al., 2014). Furthermore, a third of medical oncologists did not feel confident communicating personalised genomic results to their patients (Chow-White et al., 2017). In the context of paediatric oncology, confidence in the interpretation, use and discussion of both somatic and germline oncology testing-based genomic test results was low (Johnson et al., 2017). A recent survey found oncologists were more confident in using single-gene tests and less confident in using whole genome or exome sequencing to guide patient care (de Moor et al., 2020).

Involvement with genomics-based research and/or teaching may influence familiarity and confidence with genomics. Knowledge scores, perceived understanding and preparedness for genomic testing were higher amongst clinicians with a parallel academic role (Innocent et al., 2014). Similarly, oncologists practising outside major metropolitan areas reported less knowledge about new genetic technologies (Chow-White et al., 2017). High genomic confidence has also been associated with specific clinical roles such as being a medical oncologist or researcher-clinician (Gray et al., 2014).

4 | EXPANDING CLINICAL ROLES TO SUPPORT GENOMIC SEQUENCING

Clinical geneticists and genetic counsellors, with training and expertise in both genetics, genomics and counselling skills, are '… ideally placed to educate and support other healthcare professionals delivering genomic medicine' (Kohut et al., 2019), particularly in managing pathogenic germline variants, variants of unknown significance and secondary findings. Developments in genomic sequencing, introduction of the new GMS and expansion of mainstreaming approaches to testing in the UK are increasingly impacting the role of genetic counsellors and the context in which they practice (Patch & Middleton, 2018, 2019). More genetic counsellors are undergoing training in variant interpretation to assist in managing the vast amounts of data generated from genome sequencing (Wain et al., 2020). With genomic sequencing largely focusing on acquired variants from somatic testing, genetic counsellors may also need to develop expertise in paired tumour-normal genomics. Embedding clinical geneticists and genetic counsellors in oncology clinics and departments, possibly with supplementary oncology training, may facilitate mainstreaming approaches.

In the UK, the NHS has described nurses as being key to the implementation of the GMS across health services (NHS Health Education England, 2020); some oncology centres have already moved to nurse-led services for providing mainstreamed BRCA germline testing in breast and ovarian cancers (Percival et al., 2016). In order to support this role, nurses need strong foundations in genetics and genomics. However, research has shown low levels of genomic literacy and confidence amongst nurses in using genomics (Wright et al., 2018). Despite the development of educational resources and core competencies for integrating genomics into nursing practice (Kirk et al., 2014), key education challenges remain, such as lack of curriculum time and insufficient number of educators. Other reported barriers included limited access and resources for clinical decision support and clinical implications of genetic variation.

5 | INTERPRETING GENOMIC SEQUENCING DATA

Interpretation of genomic data is increasingly complex; the functional impact of genomic alterations—clinically relevant mutations—must be assessed for actionability and therapeutic options. Due to the complexity of reports and data produced from sequencing, misinterpretation by non-genetics specialists may lead to inappropriate estimation of disease risk and/or further diagnostic tests (Vassy et al., 2015). Genomic 'knowledge banks' which catalogue matched genomic-clinical data may support genomic data interpretation and clinical decision-making, although they do not replace expert analysis and guidance.

An emerging group of non-medical specialists who will play a key role in the interpretation and translation of cancer genomics are scientists specifically trained in clinical application of these technologies, known in the UK as Clinical Scientists (Carretero-Puche et al., 2020). With data science, computational and biomedical expertise, clinical scientists integrate genomic sequencing and clinical data producing genomic reports to inform therapeutic decision-making. These roles will be in demand in hospital settings, and close collaboration with oncology health professionals in multidisciplinary contexts is crucial to

harnessing the potential of genomic data for cancer patients, although greater recognition of this role from clinicians may be needed (Gomez-Lopez et al., 2019).

6 | NEW APPROACHES TO MULTIDISCIPLINARY WORKING

A multidisciplinary approach combining expertise from genomics, clinical genetics, oncology, pathology and clinical science is central to delivering effective, timely and high-quality care for cancer patients and families. Harnessing these disciplines via 'molecular tumour boards' (MTBs) is vital to support the implementation of genomic sequencing data in oncology (van de Haar et al., 2019). This may also impact clinical practice; oncologists reported greater confidence in interpreting tumour genome sequencing results at centres with dedicated MTBs (Gingras et al., 2016). MTBs provide an integrated setting to draw together these diverse clinical and scientific roles and encourage collaborative exchange. However, there are implementation challenges such as resource, capacity and lack of standard guidelines for MTB function, testing and tools (van der Velden et al., 2017). In the UK, multidisciplinary clinical meetings, typically comprising surgical, medical and clinical oncologists, radiologists and pathologists, are already commonplace. How MTBs could supplement, rather than be in addition to, these meetings to incorporate genomic medicine in clinical decision-making requires consideration.

This is an exciting time for genomic medicine with continuing clinical and technological advances. The implementation of the national GMS is an important step towards delivering equitable access to genomic testing and developing high quality personalised care for patients and families in the UK. One of the key factors in achieving effective integration of genomic medicine in routine care is readiness and ability of key professionals to embrace and drive this transformation. Continued education and support as well as collaborative and multidisciplinary working are essential to fully harness the benefits of genomic medicine for cancer patients.

ACKNOWLEDGEMENT

We would like to thank Dr David Church for his insight into this article.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

FUNDING INFORMATION

This work was supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this paper.

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How to cite this article: Rahman, B., Lamb, A., Protheroe, A., Shah, K., Solomons, J., Williams, J., & Ormondroyd, E. (2022). Genomic sequencing in oncology: Considerations for integration in routine cancer care. *European Journal of Cancer Care*, *31*(3), e13584. https://doi.org/10.1111/ecc.13584