

**The narrative paradox of the BRCA gene: An ethnographic study
in the clinical encounters of ovarian cancer patients**

Introduction

Over the last two decades or so, the BRCA1 and BRCA2 genes (now known to be responsible for hereditary breast and ovarian cancers) have become the centrepiece of extensive ethnographic work. As anthropologist Rayna Rapp (2014, xix) argues, in this ‘time of BRCA’ anthropologists and medical sociologists have sought to unpack the sociocultural and clinical implications of the genes. Indeed, these genes not only tell a story of ‘migration, marriage’, and suffering but also a story of gendered activism and hope as carriers of a BRCA mutation find themselves propelled into “‘imagined communities’ to militate for research and clinical resources” (Rapp 2014, xvii; Mozersky and Gibbon 2014; Gibbon et al. 2014).

It was within the context of breast cancer activism that anthropologist Sahra Gibbon’s ethnographic work, based in a UK breast cancer research charity and working in the clinical context, exposed ‘the *iconic* figure of the female BRCA carrier’ - a novel bio-social identity aligned and assembled around ‘corporeal vulnerability’, for those identified as at genetic risk of developing breast or ovarian cancer (Gibbon 2008, 21; Rose and Novas 2005, 442; Rabinow 1999). Others have examined recent shifts in the BRCA domain, as an expanding branch of scientific research known as BRCAness set out ‘on a new laboratory and clinical trajectory’; a line of research that focused on ‘clinical and molecular characteristics’, processes and behaviours found both in tumours of ovarian cancer patients who carry the germline BRCA1/2 mutations and some sporadic cancers (Bourret, Keating, and Cambrosio 2014, 177).

While the “representational figure of the ‘BRCA carrier’” continues to be an emblem of hope, particularly in preventive health interventions, and BRCAness expands our understanding of the underlying genetic mechanisms of breast and ovarian cancer, it was the progress made in the development of personalised medicine that cultivated a new partnership of hope between BRCA genomics and ovarian cancer research, as the BRCA mainstreaming genetic testing (BRCA MGT) programme was introduced into the clinical encounters of treating patients with advanced ovarian cancer (Gibbon 2008, 33; MCG 2016).

In this era of personalised medicine, this paper seeks to further the ethnographic analysis of the BRCA genes as they open up new avenues of hope to extend life in the tertiary care of patients diagnosed with late-stage ovarian cancer. It begins by exploring the sociocultural and clinical implications of BRCA MGT in the treatment setting of advanced ovarian cancer patients. The paper then turns to explore how the promise of personalised medicine shapes subjectivities in the clinical encounters of patients who carry a BRCA mutation. In this context, the paper examines how identities and technologies intersect with the themes of suffering and hope in new and contradictory ways.

By drawing on qualitative data collected during research carried out in the clinical encounters of cancer patients the author seeks to expose the narrative paradox of the BRCA gene as new hope emerges through suffering with BRCA-related cancer. Whilst this concept raises new and important questions about the changing nature of genetic risk for patients diagnosed with late-stage disease, it is beyond the scope of this paper to address these questions. Rather, it focuses on ‘the political economy of hope’

(DeIVecchio Good 2010) in BRCA to unpack its implications as it travels across and beyond the clinic. Drawing on several theoretical concepts, including Timmerman and Buchbinder's notion of 'bridging work' (2013), this paper demonstrates how hope in BRCA scales back uncertainty as it becomes part of a discourse, a method and an embodied practice across the fragile and unpredictable landscape of treating metastatic cancer.

Methods

The arguments presented in this paper are based on findings from the ethnographic study that the author primarily conducted in a gynaecology oncology clinic, which was part of a large tertiary London NHS hospital.

Participant observation was conducted across two sites. At the beginning of the ethnography, it was conducted within the 'traditional' genetic testing setting of a familiar cancer centre in two separate clinics. The initial phase of research provided an introductory feel as to where and how BRCA genetic testing is currently offered, providing key insight into the practice undertaken by clinical geneticists and genetic consultants, while also facilitating a sound comparative perspective between the two settings in which the BRCA genes travel.

Within the ovarian cancer clinic participant observation was conducted during clinical consultations between oncologists and their patients. During this time, twenty-five consultations were observed and fifteen of these encounters, with patients identified as carriers of a BRCA mutation, were audio-recorded. In addition to participant observation, face-to-face, one-on-one interviews were conducted with medical oncologists who worked in the ovarian

cancer clinic each week. Fieldwork was conducted between April-July 2016. All research material gathered was from the cancer and genetics clinics, after all NHS ethical approval had been met.

The arrival of BRCA MGT

‘I keep it on my agenda, so I have got into the habit now of making sure I put it [BRCA MGT] on the top of a summary letter...I am thinking about it for the majority of my patients now’ (Oncologist 3).

Calls for the introduction of BRCA MGT for all non-mucinous epithelial¹ ovarian cancer (EOC) patients had been steadily gathering pace over the last few years for several reasons. Firstly, diagnosing ovarian cancer early remains an ongoing challenge; symptoms of the disease are often vague, which means that many women diagnosed with the disease are diagnosed in the late stages. Most then go on to suffer relapse within two years of their initial diagnosis. Secondly, recent studies have demonstrated that up to forty-four per cent of ovarian cancer patients who carry a germline BRCA mutation have no significant family history of the disease (Hyman and Spriggs 2012). This finding challenged the traditional approach of using family history as the major selection criteria for BRCA genetic testing. Finally, and perhaps the most significant for the purposes of this paper, there has been pharmaceutical progress made in the development of the anti-cancer agents known as the Poly ADP-ribose (PARP)

¹ This type of cancer comprises over seventy percent of all epithelial ovarian cancers. This histology type is associated with BRCA mutations.

inhibitors² which target BRCA-related ovarian cancer. The pivotal turning point came during clinical trial Study 19, which demonstrated that ovarian cancer patients with a BRCA 1/2 mutation are particularly sensitive to the PARP inhibitor Olaparib (Ledermann and Kristeleit 2010). It should be noted, however, that The National Institute for Health and Care Excellence (NICE) initially rejected Olaparib on grounds of cost and questions over the potential to increase life expectancy. When it was approved in late 2015, as part of standard NHS care for ovarian cancer patients with a germline BRCA1/2 mutation as well as some patients with a somatic BRCA mutation, it was only licensed for patients who had suffered relapse three or more times (NICE 2016). This was still the case at the time of writing the paper and the implications of this decision will be discussed shortly.

Subsequently, BRCA MGT arrived in the ovarian cancer clinic at Hospital Z in 2015, two years after it was initiated by the Institute of Cancer Research alongside collaboration with selected NHS trusts. The delay in its arrival was in part due to a lack of clarity surrounding the national commissioning document and, as one oncologist admitted, the programme not being properly costed on a national scale. In fact, at the time of fieldwork, it was the hospital's charitable commission that was funding genetic testing for the BRCA1 and BRCA2 genes, to initially test two hundred high-grade non-mucinous patients. Nevertheless, patients who were offered testing - identified through

² PARP inhibitors act by blocking the DNA repair activity of the PARP enzyme, on which cancer cells are dependent. When PARP activity is suppressed, cancer cells become sensitive to PARP chemotherapeutic drugs and cancer cell death occurs.

DNA analysis of blood or saliva samples - would then receive their results in the oncology clinic, as opposed to receiving their results within the traditional setting of clinical genetics.

As scholars note, the arrival of BRCA technologies into mainstream cancer care signified a new era of biomedical practice as cross-disciplinary fields came together to share and integrate medical knowledge and practices across increasingly stratified platforms of cancer care (Bourret 2005; Day et al. 2016).

Yet, the ethnographic question that presents itself is, how did this macro-level initiative and indeed partnership between BRCA genetics and oncology unfold in the micro dynamics of treating patients with late stage disease? In what way did it shape the subjectivities of those delivering this technology?

During interviews with oncologists it became clear that BRCA MGT carried with it three key benefits. First, identifying a mutation opened up the possibility of testing unaffected family members; offering risk-reducing surgery and screening to help prevent future cancers. Second, as oncologists explained, identifying a mutation gave them some idea of how well patients were going to respond to standard first line platinum-based chemotherapeutic treatments. Third, identifying a mutation allowed them to make targeted treatment recommendations, such as access to Olaparib, which as noted earlier had recently been approved by NICE.

Despite a simplistic overview of the benefits of BRCA MGT, as the opening excerpt to this section suggests, testing generated a scaling-up of care as oncologists went about

their daily practice. Nevertheless, as oncologists reflected on the arrival of BRCA MGT, it became clear that in addition to its benefits, oncologists were also confronted with the somewhat unusual task of finding the right time to introduce genetic testing into an already busy and particularly challenging encounter. As one oncologist told me, ‘Patients might be receiving another line of chemotherapy that they are familiar with, so they know what to expect...they don’t have too many problems to raise... that would be a good time to do it’ (Oncologist 3).

Along similar lines, this soul-searching was further clarified by as another oncologist who also reflected on when they felt was the best time to raise the prospect of testing:

‘I will raise the question of BRCA testing near the beginning or at the beginning of the consultation for the newly diagnosed patient. I will then leave it. Then come back to it, come back to it again, come back to it again. By the time we come back to it a third or fourth time, towards the end of chemotherapy, then the patients are familiar with it, it is not a new topic. It is just they have so much to deal with right at the beginning, to do the testing right at the start, I think is tough’ (Oncologist 2).

The oncologist’s thoughts here not only reflect the fragile terrain within which BRCA MGT has arrived but the way in which the potentiality of BRCA genetic testing was shown to have acquired a somewhat unconventional present/absent character, as oncologists sought to minimise overburdening their patients with further treatment decisions. Indeed, as the technology travels a non-linear trajectory, layers of intersubjective communication must be woven into the clinical interaction, which not only inform the technology in oncology but transform it into a highly moralised and deeply reflexive practice, as oncologists must wait, allow time, provide space to

introduce, revisit and revisit again the meaning, value and potential hope in BRCA MGT.

Nevertheless, although interviews with oncologists offered important insight into how BRCA genetic testing shapes and is shaped by the subjective experiences of oncologists, due to the infancy of BRCA MGT in Hospital Z, and limited funding, no such clinical encounters were observed in which BRCA MGT was in fact raised.

Hence, the focus shifted to those patients who already knew of their BRCA-positive status. As the focus shifted, it became clear that testing for a mutation involved something more than merely an additional diagnosis which generated new methods of treatment and modes of reflexive practice. Rather, in the move to develop and deliver personalised medicine, the BRCA genes are not only central to the ‘political economy of hope’, but have become a key tool and instrument of change that reconfigures the “‘local’ culture - symbols, constellations of meanings, and forms of discourse that reflect and organize” modern ovarian cancer care (Geertz (1983) as cited in DelVecchio Good et al. 1990, 60; Rose 2007).

Before exploring this argument in more depth, it is important to take a step back for a moment to understand how and why the concept of hope in oncology has, itself, been transformed. Until recently oncologists had fewer treatments to offer their patients. As one oncologist admitted:

‘...so... it’s been pretty much the same, so the two drugs that we use all the time have been the same for a decade, carboplatin and paclitaxel, we treat with loads and loads ...we do that more than anything else.’

Thus, previous decades, aside from standard chemotherapy in clinical practice, saw few if any personalised therapeutics coming to the fore. As a result, oncologists tended to view and speak about ‘hopefulness in more general clinical terms than contribution to longevity’ (DelVecchio Good et al. 1990, 70). Indeed, during this time the narrative of hope was seen as a way to instil an more optimistic attitude in patients. This conceptualisation of hope reveals not only its somewhat fragile nature but stands in sharp contrast to its present-day orientation. As Rose and Novas (2005) argue, in the post-genomic era the ‘political economy of hope’ has been transformed by a series of innovative biomedical factors (454). For example, the increased in efficacy and decrease in cost of genomic sequencing, has fuelled biotechnological innovation. Furthermore, as they note, a new commitment to learning and knowledge production at the molecular level demonstrates that ‘biology is no longer blind destiny ... it is knowable, mutable, [and] improvable’ through the manipulation of damaged genes and the development of personalised drugs, such as Olaparib (ibid. 2005, 442). In this respect, a new narrative of hope is generated not only through the patient’s genetic identity but also through its ‘measurable impact on the biology of cancer’ and potential partnership with personalised therapeutics that can extend life (Delvecchio Good et al. 1990, 72).

It is to this evolving milieu of hope that we now turn our attention in order to consider how and why the approval of Olaparib by NICE ignites the ‘medical imaginary’ across and beyond the clinic (DelVecchio Good 2010, 273).

Better to be a carrier?

The licensing in Europe of the first PARP inhibitor, Olaparib, in 2014 was heralded as a milestone for the provision of targeted cancer treatments. As stakeholders from across the board pointed out, Olaparib became a symbol of hope for relapsed ovarian cancer patients who carry a BRCA mutation. In fact, despite NICE's initial rejection of the drug, its subsequent approval confirmed that the last decade or so of economic and cultural investment in the BRCA genes had paid off, as Olaparib was touted as one of the first personalised therapeutics to enable BRCA-positive women to live longer in remission.

As Mary DelVecchio Good would argue, Olaparib enveloped oncologists and patients in a 'biotechnical embrace' (2010, 275); a term she coined during her international ethnographic work on the culture of oncology to describe 'the subjective experiences and affective responses of many clinicians and their patients when using new biotechnologies' (2010, 275).

While DelVecchio Good's ethnographic work captures the way in which high technology treatments and promissory cancer trials (something which will be discussed shortly) invite patients and oncologists to live in the ever-present spaces of hope and progress, her research, along with other cancer scholars, illuminates not just the human cost and deeply precarious nature of cancer therapeutics but also the way in which the actual patient experience is often 'missing from these accounts or papered over with epithets of their bravery and courage' and their hope for the future development of anti-cancer agents (Lochlann Jain 2010, 93).

Somewhat similarly, whilst the approval of Olaparib energized the upstream investment in personalised medicine, downstream the narrative of hope to extend life for BRCA-positive patients was restricted by NICE guidelines which dictate that patients must wait until a third relapse before accessing Olaparib.

The rigidity of the current framework raises social and ethical concerns as patients are propelled into an uncertain and highly distressing trajectory of prolonged liminality, as they become ‘patients-in-waiting’ to access a potentially life-extending drug (Timmerman and Buchbinder 2013, 67). This point is important for thinking through if or how hope in innovative drugs, like Olaparib, translates and transmutes as it travels into the micro-dynamics of the clinical interaction.

Indeed, what type of emotional work and affect is woven into an ‘embrace’ of a drug that transforms patients into patients-in-waiting to relapse? How do such constraints restrict and or (re)structure the imaginative possibilities and hopes of those living with late-stage disease?

It is from this perspective that we now turn to focus less on the molarity (Deleuze and Guattari 2013) of hope in BRCA. Such a macro perspective pays less attention to, and thus, offers little insight into, the twists, turns, and shifting ontological nature of hope, which is captured in the following ethnographic excerpt between Emily and her oncologist.

Emily

Emily, a BRCA2-positive patient in her early sixties, was diagnosed in 2010 with Stage 2 EOC. She has suffered relapse on two occasions and has returned to

discuss re-starting treatment as she fears that the cancer is slowly ‘on the move’ again. It’s over six months since her last course of chemotherapy and as the excerpt reveals, she expresses deep unease in just waiting for cancer to make itself visible. As the conversation begins, it soon gravitates towards discussions of how best to ‘move forward’ to speed up Emily’s access to Olaparib.

O: So we did the scan in March ... So, I guess the thing about scans is that it doesn’t always see everything, particularly if there is something new happening ... how long have I been monitoring you now off treatment?

E: Long enough.

O: It’s about six months, is it?

E: More than that, isn’t it?

O: When did we know there was something was back....?

E: October, the CA125 went up... And I just feel I need to get on with it.

O: I am sort of feeling the same...

E: Is there anything to say that I shouldn’t?

O: Exactly... there isn’t. The reason for getting on with it is we know that you can then get Olaparib afterwards, because this is third line chemotherapy for you. So Olaparib is available ‘at the moment’ [my emphasis] on the NHS, if you have got a BRCA mutation... So you tick all the boxes... So, I think in some ways it is safer to get on with that before anything changes and they take it [Olaparib] off availability again.

E: Do we need the CT scan?

O: No... as I know that things are...

E: Slowly growing.

O: On the move.

Patients identified with a mutation must wait patiently until they have met NICE eligibility criteria to access Olaparib. However, explicit in this dialogue is the felt experience of being structurally stuck in this position. As Emily recounts her embodied unease in having to wait to relapse, the narrative reveals a sense of urgency to address the creeping up of cancer. Moreover, it is the clash between macro-level restrictions and micro-level dimensions that prompts her oncologist to make a subjective yet calculated

clinical judgment to ensure that those who tick all the bureaucratic boxes gain access to this life-extending drug.

The excerpt not only draws attention to the complex ways in which hope in BRCA shapes subjectivities in the narrative process, but also to the way in which the genes are transformed into a highly performative tool; one that repairs ruptures and restores hope through the creation of a novel form of BRCA ‘therapeutic citizenship’ (Nguyen 2005, 126). In this respect, the genes are not only performative but culturally productive, as they restore a sense of order to the chaos of cancer and create a new and hopeful therapeutic identity that lends itself to a form of resistance against the volatile and deadly terrain of living with and treating metastatic cancer (Kleinman 1988).

While Emily’s encounter captures the varied and complex processes of shaping subjectivities and identities through the ‘affective economies’ of hope and progress, in many encounters I observed with BRCA patients, there was also an explicit acknowledgment of the gaps in knowledge, ambiguities, and unintended consequences unfolding around BRCA technologies (Lochlann Jain 2010, 93); for instance, oncologists openly admitting uncertainty as to how long Olaparib will be available on the NHS, or the problematic nature in relation to tracking such an insidious cancer. Each uncertainty created moments of improvisation and revision, which spoke clearly to Timmerman and Buchbinder’s (2013) analytical concept of ‘bridging work’ as oncologists sought to sustain the story of hope in the genes as they became woven into the uncertain world of oncology.

The term bridging work was originally conceived during Timmerman and Buchbinder's ethnographic work, which examined the consequences of implementing population-based new-born genetic screening across the US. The concept refers not only to the work undertaken in the genetics clinic to 'reconcile the promise of new technologies with the realities of their implementation' but also to the way in which clinicians 'bridge the ontological gap between pre-and postscreening knowledge' as technologies often generate what they describe as 'anomalies' and 'unintended consequences' (Timmerman and Buchbinder 2013, 63, 98, 64).

Somewhat similarly, following the arrival of BRCA MGT, the notion of bridging work calls attention to the enhanced levels of reflexivity and intersubjective communication demanded as oncologists seek to construct a bridge between deep suffering and the novel, albeit contradictory, discourse of hope unfolding around the BRCA genes. Equally, oncologists must construct a bridge between the hope in the drug's potential to extend lives of patients with the reality of its implementation; that is, how NICE guidelines transform BRCA patients into patients-in-waiting to relapse for a third time.

Yet, what was particularly striking was the substantive amount of bridging work undertaken to obscure, or rather, smooth over gaps in BRCA knowledge, as hope in BRCA stretched into each corner of the clinic; from surgical outcomes to clinical trial research, as well as the overall management of the disease with Olaparib.

The following vignette between Sarah, a BRCA1 patient, and her oncologist illuminates the juxtaposition between the faltering in knowledge and the scope of hope in BRCA as they consider the possibility of further surgery:

‘Because of your BRCA mutation, you are in a better biological category.... We think we have a lower threshold to do surgery in patients who have a BRCA mutation. Even if there are just one or two specs of disease, there is a different biology at play, which means that the disease doesn’t seem to spread quite. It’s just a different biology in surgeries but has more of a role. Okay?’ (Oncologist 2)

Each example above illuminates the nuanced and often profound processes of bridging work unfolding across the clinic. Yet, the oncologists’ comments here also elucidate what I term the ‘narrative paradox of the BRCA gene’ as they travel from the field of preventive genetic testing into the practices and techniques of oncological care. Indeed, contrary to the narrative of risk of developing cancer, which consumes the BRCA genes in the field of preventive medicine, within the clinical encounters of oncology, where cancer is now realised and patients face the risk of disease progression, the BRCA genes have become infused with an explicit positive performativity; conveying a sense of hope where patients in receipt of a mutation may fare better than those situated outside of that better BRCA biological category. As such, when translated into, for example, access to innovative anti-cancer agents or surgical expertise, the BRCA genes become an affective and important mechanism that makes a potentially positive difference to treatment outcomes and even overall prognosis. It is within these contradictions that BRCA-positive ovarian cancer patients too must grapple with the narrative paradox of the BRCA gene, as their embodied sense of suffering with cancer - because of their mutation - turns into a source of hope and indeed a powerful tool in efforts to control their cancer.

It is within these contradictions and gaps in knowledge concerning the role of the BRCA genes that the concepts of ‘translation and transmission’ are useful to understand and rethink how technologies, knowledge and BRCA patients are becoming increasingly woven together in new and innovative ways (Gibbon 2007, 189).

In their analysis of transformations of cancer patienthood, Ann Kerr and Sarah Cunningham-Burley (2015) have written extensively about the social impact, emotional work and affect such biomedical advances and innovative technologies have upon patients. They pointedly note that the increasingly borderless boundaries between research and clinical practices means being, all at the same time, ‘a patient, a research participant and a good biological citizen’, each of which carry ‘emotional work to handle the conflicting sense of responsibilities and rights involved’ (Kerr and Cunningham-Burley 2015, 193; Cooper and Waldby 2014). Likewise, developments in trials and new personalised therapies mean that more than ever is demanded of the cancer patient, as each technological embrace demands a heightened means of engagement which extends far beyond the notion of ‘patient participation’ but rather signifies what Kerr and Cunningham-Burley coin as ‘embodied innovation’ (2015, 203).

Indeed, as patients articulate their embodied experiences as well as the psychological effects of taking life-extending technologies, and companies gather data on patients’ differing responses, scholars increasingly question who benefits from the cumulative entanglements between technologies, patients and innovative techniques (Lochlan Jain 2010; McMullin and Weiner 2008).

In discussing the politics of the randomised control trial (RCT), Lochlann Jain notes how ‘the hegemonic tropes of hope’, charity and survivorship, not only obscure ‘cancer’s profitability and scientific uncertainty’, but most importantly, the deep suffering and cost of individual lives needed to sustain trials (2010, 94, 91). Certainly, the stories that unfolded in the clinical encounters between oncologists and their patients, who had endured multiple courses of chemotherapy and live in hope to be selected for recruitment onto innovative trials, revealed how the desire for cure often downplays or misrepresents suffering in the clinical narrative.

Interestingly however, the observations with BRCA patients revealed less a hierarchy between suffering and hope than a striking duality of processes unfolding between the two. Oncologists sought to craft a narrative which managed the suffering and trauma of cancer - as a consequence of a BRCA mutation - while communicating a new-found optimism and hope to those BRCA patients caught up in the experimental possibilities of BRCA research.

Most notably, the interplay between suffering and hope was most striking for those BRCA patients caught up in the evolving landscape of personalised medicine. Discussions in the clinical encounters with patients taking Olaparib not only offered unique insight into how hope in BRCA technologies have become entangled in ‘the phenomenology of living’ and suffering with metastatic disease but also revealed how women sought to understand suffering through the lens of living on and with a drug that she hopes will lengthen her life (Bell and Ristovski-Slijepcevic 2011, 645).

It is to this group of patients, for whom Olaparib has become a reality, that we turn to examine; not only the difficulties and daily efforts to manage suffering while sustaining hope in the goal of the drug, but also the increasingly malleable and creative nature of the work undertaken within the politics of personalised medicine.

Hoping to live for longer

During fieldwork, given the recent licensing and eligibility criteria surrounding Olaparib, I observed few patients who were indeed taking Olaparib. Nevertheless, Sally, a BRCA2-positive Stage 3 patient was one of the few I managed to observe. As she embarked on a new way of living on and with Olaparib - from standardised chemotherapy to daily oral targeted maintenance therapy - the exchange captures not simply the physical and emotional effects of the drug, but the expectations surrounding personalised medicine as it becomes part of standard care.

Sally

O: So how did you find the first cycle?

S: Tough.

O: In what way?

S: I did vomit after my night pills. They all used to come out...I think three times.

O: Three times. In the first week?

S: The first two weeks were worse. It is getting slightly better. The only thing... it's so uncomfortable, the digestion if I eat... Some things like tea, I used to drink lots of cup. I don't like the taste...nothing tastes as good, but it's getting better. I have a horrid taste in my mouth after eating throughout the day. I'm still very tired.

O: So, you are giving me all the normal side effects.

S: Oh right. I just hope my quality of life gets better. That is the only thing I'm worried about.

O: Exactly.

S: Because I'm quite an active person. So I'm just a zombie at home at the moment.

O: So that's absolutely not what we want. ... The tiredness, your blood counts are fine... There's no significant anaemia... the taste change, again, that's something that I hope will just get better over time...

S: Oh right, that's good.

As the exchange illustrates, the opening question, 'So, how did you find the first cycle?' elicits strong emotions from Sally, reflecting her frustration at a diminishing quality of life caused by the first cycle of the drug. Whilst Sally's oncologist is sympathetic to her suffering, her response offers important comparative insight into the way hope, suffering, technologies and identities are woven together and pulled apart across the evolving landscape of personalised cancer care. For example, in the case of Emily's encounter, in order to address her deep sense of suffering at having to wait any longer, her forthcoming scan is separated out and put to one side of the clinical narrative, making a new and hopeful space through which potential in Olaparib can be materialized; whereas, in Sally's encounter, objective technologies of surveillance, such as blood count measures are not only foreground but drawn upon to normalise and, indeed, explain away her sense of suffering as something entirely expected that will improve over time.

Collectively, the two encounters are significant for thinking through how hope, genetic identities and investment in BRCA technologies not only shape subjectivities but reorganise values, as suffering is brought in and out of recognition to buffer unanticipated consequences, scale back uncertainty and thus maintain the hope in Olaparib as it becomes routinized in the clinic.

Yet, as oncologists seek a fine balance between providing a sense of normalcy while remaining vigilant and attentive to their patients' suffering, inevitable slippages occur. As the conversation between Sally and her oncologist continues, the prospect of a dose reduction is raised:

O: ... Obviously... if things don't gradually improve over the next cycle... then we'll consider a dose reduction.

S: I don't want that. But if we have...

O: If we have to, we have to.

S: Does it make a difference?

O: Well, ...we need to look at it ... that we need to tailor the dose. This is a flat dose recommended for all people ... If we have to go down to 100mg twice a day then we probably are compromising the... drug. But just going from 400 to 300 twice a day I don't think is too much of an issue... I think it's worth pressing on...

S: That's why I want to take it.

The shift from optimism and hope to a more guarded and sombre warning allows us to revisit the notion of 'bridging work' once more; as potential change on the horizon in relation to Sally's dose demands ever more creative interventions 'through the shifting of the norm itself', hope is thus preserved that a reduced dose of 300mg would not be too much of an issue (Timmerman and Buchbinder 2013, 142). This turn to creativity is therefore one to uncomplicate bodily matters, to provide a sense of clarity and resubstantiate hope within shifting knowledge-practices. Yet, the narrative of hope in personalised medicine also tells another story.

In the final moments of Sally's encounter, as she relays her worries that she may not be able to take Olaparib at her 'set times' due to an essential trip abroad, the oncologist's comment, 'You should take them, because I think it will be fine. I think you will be safe with them', reveals not simply an expectation and perhaps even a new obligation placed upon the BRCA therapeutic citizen to make time in their daily routine, but a new moral claim that doing so will keep patients like Sally safe. In this framework, hope in Olaparib invokes something far greater than just adherence to novel treatment strategies to hold back late-stage cancer. Rather, this paper suggests that personalised medicines, such as Olaparib embody a new moralism; one which not only

cultivates a culture of safety but provides patients like Sally with an emotional sustenance that carries with it a profound sense of trust and hope in the drug as it is woven into the fabric of their daily lives.

The way in which the properties of moral value and safety are woven into the discourse of hope convincingly redirects our attention to scholarly interest examining the role of affect and the emotional work these practices afford. Walkerdine's (2010) important work and engagement with trauma, affect theory and 'the concept of the unconscious' amongst an 'ex-steelworker community' in South Wales illuminates how certain practices and 'relational dynamics...experienced through the senses and operate within a pre-verbal register' enable the community 'to retain a sense of togetherness in the face of the decimation of the industrial modes of working' (Blackman and Venn 2010, 18, 19, 18). Although far from a clinical environment, Walkerdine's approach to understanding affective dynamics at play, and the way in which 'material objects, such as the steel-works' - and in the context of the clinic, innovative therapeutics like Olaparib - can 'be thought of as psychic objects', not only teases out the 'relationships between bodies, affect and life' but also how the 'spatial configurations' of material objects 'can amplify particular affective dynamics... or even destroy' notions of safety and trust that are nurtured across time within close-knit trusted relationships and communities (Blackman and Venn 2010, 20, 18, 20). Walkerdine's ethnography, along with the work of other scholars, highlights important connections between the material, symbolic and semiotic meaning of particular objects across landscapes (Carroll and Parkhurst 2018; Reynolds Whyte, van der Geest and Hardon 2002).

In the context of the clinic, the materiality of medical objects such as Olaparib raises important questions about how their material essence and aesthetic quality stir up

particular kinds of emotional work and embodied response in patients propelled to the frontline of developing cutting-edge personalised medicine.

Although it is true that a growing population of BRCA ovarian cancer patients is actively involved in and affected by the production and refinement of these innovative drugs, due to the unpredictable and deadly nature of late-stage disease for many BRCA patients, their role as embodied innovators and the hope invested in their BRCA genes has yet to be realised. The hostile environment of treatment failure and tackling drug resistance seemed to push the hope so clearly practiced around Olaparib into the realms of ‘salvage therapy’ (DelVecchio Good 2010, 277).

It is to these patients that we now turn our final attention, as hope in BRCA becomes woven ever deeper into the exploratory ground of clinical trial research.

Attending to Imaginary Futures of the Clinical Trial

Most scientists, clinicians, and many patients too, claim that randomised control trials (RCT) - a double blinded clinical cancer trial whereby patients are separated into two groups and administered different treatments in order to measure the efficacy between the two - are not only ‘the gold standard of evidentiary medicine’, but have led to an exponential increase in cancer survival rates as a result of their capability to determine new treatments (Lochlan Jain 2010, 95; Keating and Cambrosio 2012).

Indeed, Hospital Z was renowned for its large portfolio of clinical trials. As one oncologist explained, ‘We have a big trial portfolio, and always do... so whenever I see a patient that is what I am thinking - is there a trial for them’. At the time of fieldwork, there was a tangible sense of anticipation and hope circulating in the clinic, as the long-

awaited first immunotherapy clinical trial was soon to be conducted. As one oncologist enthusiastically told me, ‘Immunotherapy is a big deal for all cancers. We are yet to find out for ovarian cancer how we can utilize the immune system therapeutically, but immunotherapy is a big deal, just hot throughout cancer’.

Most notably, this palpable sense of hope in the imaginary possibilities of immunotherapy was particularly pertinent for the BRCA patient who had developed drug-resistant disease. As one oncologist explained to her BRCA1 patient Suzie, who was about to embark on another gruelling course of chemotherapy (following the news that her cancer had returned and spread extensively), ‘So, we’ll do this and then I think we consider an immunotherapy trial and having a BRCA mutation is a good thing for immunotherapy ... You’ve chosen the right thing’.

Similarly, the hope now positioned between the BRCA genes and immunotherapy was illustrated again in the discussion between Daniela, a BRCA2 Stage 4 patient who had not long been battling breast cancer, and her oncologist. After giving Daniela the bad news that the trial was ‘on hold’, her oncologist sought to address Daniela’s obvious despair while reiterating her commitment to and hope in immunotherapy, as she rather apologetically confessed, ‘it’s been slower than we anticipated I am sorry... but I am advising you, what is best for you... and I think it is best to have the immunotherapy next’. Indeed, after a long and tense discussion, her oncologist’s final words ‘...we have got a plan... so we have just got to stick with it’ clearly illustrates the emotional investment and future hope that for those, as one oncologist put it, with a ‘mutational load’, immunotherapy treatment would prove particularly beneficial.

Of course, the full potential of the BRCA genes in immunotherapy ovarian cancer research remains to be seen. Nonetheless, these discussions suggest that for those like Suzie and Daniela, who find themselves situated in a perilous in-between moment, hope in BRCA has a new-found ‘freedom of referential activity: one whose direction’ is neither contained in the present nor contingent and controlled by past trial success (Lochlann Jain 2010, 105). Moreover, it could be argued that hope in BRCA has acquired a distinctive prospective orientation towards what philosopher Ernst Bloch describes as the ‘not-yet’ moment, as it travels into the unproven and uncharted landscape of immunotherapy research (Miyazaki 2004, 14). Even though Bloch’s concept of the ‘not-yet consciousness’ was originally conceived in his seminal work *The Principle of Hope* (1995) to address what he perceived as philosophy’s ‘retrospective character’ (Miyazaki 2004, 14, 130) - that is, its inability to understand ‘the world [as an entity] full of propensity towards something’ - the concept resonates with how the imagined chemistry between the genes and immunotherapy technologies serve as a catalyst for the reorientation of hope in what lies ahead (Bloch 1986, 18 as cited in Miyazaki 2004, 13). From this angle, hope in the BRCA genes is now fashioned around and contingent upon ‘a prospective momentum entailed in anticipation of what has not-yet become’ (Miyazaki 2004, 14).

Furthermore, in contrast to earlier scenarios where hope is preserved through the containment of uncertainty, at the margins of hope, it is paradoxically the uncertain nature of the dynamics anticipated to materialise between the genes and immunotherapy research that has become the creative resource and instrumental tool to generate hope in what lies ahead. From this perspective, the uncertainties that surround the genes not

only bridge the gap between suffering and hope but extend that bridge into the realm of the medical imaginary that is ‘open to mystery, potency and change’; that shapes the subjectivities and behaviours of oncologists, and most importantly BRCA patients, who live in hope of becoming part of the expanding group of embodied innovators in the story unfolding around the BRCA genes in ovarian cancer care (Good and DelVecchio Good 1994, 837).

Conclusion

Drawing on ethnographic research, this paper has sought to illustrate how a BRCA mutation is not simply part of a clinical strategy focused on identifying and thus treating patients according to their molecular profile. Rather, a mutation is central to the political economy of hope that bridges the gap between life-threatening illness and the hope of extending life. In the context of extending life through the development and delivery of personalised medicine, this paper hopes to have exposed the wider social importance of the genes, which not only speaks to individual but collective hope to improve the quality and quantity of life by transforming cancer from a life-threatening disease into a chronic condition.

Beyond highlighting the work involved to stabilize and indeed generate hope in BRCA, I have sought to expose the emergence of the narrative paradox of the BRCA gene – that is, how the negative potential in the genes to inflict often multiple cancers upon those who carry a mutation has become transformed into a positive mechanism and an important tool amongst the armamentarium of oncology.

At the same time, by shining a light of hope on the genes in this way also reveals

how shadows are produced across the clinic. Indeed, although hope in BRCA opens the door for some, it remains firmly closed for many others. Thus, the new chapter in the BRCA story brings fresh challenges and new meaning to all those affected by the disease, which opens up a new space for future anthropological work to explore the ever more complex relationships and entanglements, as the genes, technologies, and identities intersect with the themes of suffering and hope in new and contradictory ways.

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Ethical approval

This research was given ethical approval by NHS Research Ethics Committee (REC) in the UK.

In accordance with Taylor & Francis and my ethical obligation as a researcher, I am reporting that I have no conflict of interest.

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