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## Figuring Molecular Relapse in Breast Cancer Medicine

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### Introduction

Medical practice and research in oncology increasingly involve and respond to highly various and heterogeneous disease classifications, which evolve with time and in response to emerging programmes of treatment and research. These reflect novel practices that produce different forms of risk prediction and risk analysis. Supported and facilitated by translational research programmes, trials networks, and interoperable

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data sharing platforms maintained by diverse collaborative groupings, there has been a proliferation of breast cancer subtypes and treatments (Day et al. 2016; Cambrosio et al. 2018; Bourret et al. 2021; Day et al. 2021). During an ethnographic study of personalised breast cancer medicine and healthcare in a London hospital (2018-2021), members of a research group of which we are members learned that research in tumour biology is highly complex (Day et al. 2021; Day, Smith and Ward, chapter 8, this volume; Viney et al. 2022). And while treatment for primary disease is increasingly effective compared to other tumour types, especially when treated at an early stage (Cancer Research UK 2021), the return of cancerous cells after the treatment of a primary tumour—known as a ‘recurrence’ or ‘relapse’—can be difficult to predict for individual cases. It is cancer’s uncertain return, its temporality, and the figures its times generate that is the subject of this chapter.

Cancer cells have been observed in human blood since at least the later nineteenth century (Ashworth 1869). Fragments of cell-free nucleic acids in human blood were first described in the 1940s (Mandel and Metais 1948), and cfDNA was identified and associated with cancer in the mid to late 1970s (Leon et al. 1977). The serial measurement of these and other biomarkers has long provided hope: “sequential measurements of DNA concentration may be a useful tool for monitoring the effects of therapy” (Leon et al. 1977: 650). The promise contained in this ‘may’ is just one temporal effect of liquid biopsies, which have been made to occupy the future anterior tense,<sup>1</sup> which we argue anticipates figures and generates figures to be retrospectively (Brown and Michael 2003). Considering these figures allows a greater appreciation of how cancer research places and transfigures disease, placing it in time, and making it ‘historical’. The study we focus on here figures the relapse of disease for patients treated for breast cancer and who are classified as being at high risk of developing metastatic recurrence. Our engagement with this study occurred when the scientific research group published early findings, and, fortuitously, we were able to observe how scientific findings were being

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<sup>1</sup> Some liquid biopsy studies now track cell-free and circulating tumour DNA in time-based practices: ‘early’ and ‘earlier’ and ‘just in time’—so resonating with precision practices in other domains. As a consequence, liquid biopsies represent enduring promissory figures—‘soon’ and ‘not yet’—that herald improved patient outcomes.

made public. We noted how concepts of disease and the people associated with disease were being figured by these figures. We wanted to learn how people and groups of people are incorporated and at times excluded by numbers, images, and texts. If figuration is a methodological practice, this chapter reports on figures as objects of discovery and description and, concurrently and in combination, as epistemic and symbolic matters of concern.

During our research, in formal and informal interactions with clinical researchers, we learned that, at molecular levels now explored via contemporary diagnostic and treatment technologies, tumour biology does not usually conform to easily predicted norms and averages. As one oncologist explained as we began our interviews, “we’re in this era where it’s expanding the varieties and number and types of cancer due to the molecular characterisation of each patient’s cancer ... virtually every patient has a different type of cancer due to the genetic changes that occur in the cancer compared with normal tissue.” Their colleague in oncology summarised: “there are no more averages. I can quote averages from clinical trials, but we don’t know.”

One promise of a more ‘personalised’ or ‘precision’ medicine is that recommendations will provide ‘the right treatment, to the right person, at the right time’ (Keogh 2015; Scoltz 2015). Despite this promise, tools to enhance precision and prediction in oncology move by contingent increments, where definitions of ‘right’ change gradually. Different scales and speeds of implementation and impact can be narrated from different situated perspectives. Narrating these diverse perspectives on ‘targeted’ approaches to oncology is not easy with the views of patients and staff varying widely. One claim of this chapter is that understanding developments in translational medicine might be aided by documenting and discussing how figures are made and maintained by different actors involved in this work of targeting. Patients, clinicians, biomedical, and other kinds of researchers make and interact with these figures, and they comment, evaluate, and form expectations about figures. In this chapter, figures are an empirical proof and promise in ways that are at once confirmatory and confounding. In precision oncology as in other fields, figures are contested and can attract conflicting values based on different interpretations of their performance.

## Background to 'An Exploratory Breast Lead Interval Study' (EBLIS)

One approach gaining popularity among biomedical researchers in oncology involves monitoring the presence of tiny fragments of cell-free DNA (cfDNA), some of which can be associated with tumour cells known as circulating tumour DNA (ctDNA). The practice of detecting and analysing ctDNA in fluids for diagnostic purposes is called 'liquid biopsy'. Liquid biopsies are created to detect, measure, and analyse disease in a minimal, residual state. Researchers use genomic and other omic sequencing techniques to identify these molecular signs of disease and, in oncology, disease recurrence. While temporal horizons of risk are currently formed for individual patients based on data using population averages or norms that contribute to the formation of groups and sub-groups of patients, research studies tracking ctDNA adjust the practice, scale, and the horizon of relapse using molecular data from individuals. This approach detects and tracks micrometastatic cells in ways that are molecularly specific to individual patients, illuminating *when* disease relapses by reducing the question of *who* is affected to a single person, and opening new opportunities for learning *why* cancer returns.

As part of our work in the hospital service, our research group followed the progress of one observational study tracking ctDNA in a group of breast cancer patients: EBLIS, an Exploratory Breast Lead Interval Study. We were told by a clinical researcher involved in EBLIS that the study represented the only example of personalised breast cancer medicine in this London breast cancer service. Previous work by members of our research group have documented changes to how clinical practice and research is conducted in this service (McGrath-Lone et al. 2015; Day et al. 2016; Day et al. 2021; Viney et al. 2022). As a translational research study that follows a cohort of patients whose primary treatment had concluded, the status of EBLIS as a unique example of personalised medicine intrigued us. Motivated to learn more about this work, we followed study participants, clinicians, researchers, administrative as well as patient samples, and data over time and across different sites, following a process of data making and circulation, analysis, and communication.

Our observational and interview research followed EBLIS towards the end of its initial four years of activity. In total, 194 breast cancer patients had been recruited from 3 UK clinical sites (1 October 2013—8 July 2016). Out of which, 188 were tracked for the first 4 years of the study. While this group of patients constituted a group or cohort they were not recruited based on shared biological or therapeutic characteristics. And patient-participants were varied in terms of age at diagnosis, histology, hormone receptor status, and treatment. But all patient-participants shared in risk categories—numeric values that related them as a group to a near but imperfectly known future. They were at high risk of clinical relapse based on a digital risk prediction tool called *Adjuvant! Online* (see de Glas et al. 2014; Lambertini et al. 2016). Here ‘high risk’ was defined in terms of risk of mortality equal or greater than 50% at 10 years without therapy, or corresponding to a relapse rate of 65% at 10 years without treatment. While EBLIS generated novel numbers for clinical researchers, this was possible because it was embedded in existing practices of clinical figuration. This wider scheme of figure-making between existing, emerging, novel and established material occurs at many scales, and the dynamic temporalities of making ctDNA a clinically actionable biomarker will become clearer by describing the circulation and combination of different figures of disease.

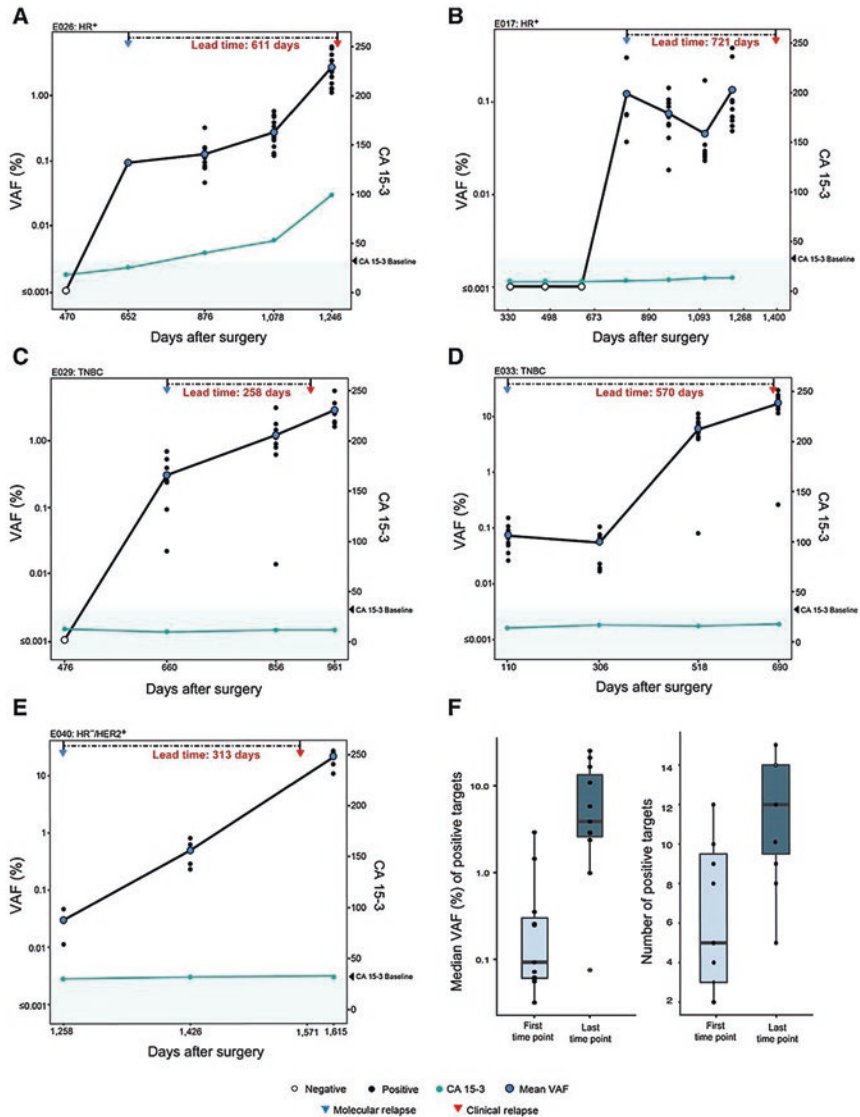
At the beginning of their care in the hospital, patient-participants provided a sample of their tumour. This sample was used by researchers to specify the molecular profile of their primary disease, using a range of next generation—omics sequencing technologies. Researchers leading EBLIS collaborated with a US biotechnology company to create a “bespoke amplicon design pipeline” that nominated PCR primer pairs for a given set of genetic variants. In brief, somatic variants were identified at a patient level, pairing the primary tumour sample with matched white blood cells using whole-exome sequencing (WES). Each patient’s tumour was attributed a signature, composed of 16 highly ranked pieces of genetic code selected to create a “custom patient-specific panel” of mutations. Subsequently, the clinical research group collected blood samples at six-month intervals and checked this against the patient-specific panel, to track and measure changes in the volume and characteristics of ctDNA over time. The study therefore developed a ‘personalised’ analysis

insofar as it tracks disease at molecular, patient-level and patient-specific conceptions of disease progress. Each patient participant in EBLIS has had their tumour sequenced in a way that is specific to their tumour characteristics. They are then followed on the basis that they are unique, each patient participant providing their own baseline for an evolving sequence of testing and retesting.

Approximately 6 months into our fieldwork EBLIS reported its design and results, providing information for the first 49 patients who had relapsed since consenting to be part of this research study. Appearing in *Clinical Cancer Research*, these results were published in April 2019 (Coombes et al. 2019). EBLIS had set out—among other things—to bring more predictive certainty to recurrence, and this publication uses diagrammatic reasoning to present its experimental findings. It did so with a set of contrasting figures, expressed in diagrams, plotting somatic changes of emerging experimental interest against common clinical biomarkers and screening technologies used in the NHS. It visualised a new temporal event or horizon in order to present and illuminate an otherwise obscured object of clinical interest: a threshold number of ctDNA that declares cancer's return. By tracking ctDNA, the group suggest the clinical utility of “molecular relapse”, which they separate from “clinical relapse”, a term used to denote recurrences discovered through existing screening systems and technologies.

The findings summarised and plotted in diagrams suggest an ability to detect a recurrence up to 2 years ahead of existing screening technologies (median=8.9 months; range=0.5-24.0 months). The diagrams (see Fig. 7.1) are works of figuration that gather, propose, and represent this novel event as a temporal interval by contrasting molecular and clinical relapse, demonstrating the potential usefulness of one figure in contrast to another. More generally, the study uses, enacts, and contrasts many figures: its work of figuration has many dimensions and horizons, with these two-dimensional diagrams used to picture cancer's progression central among them.

One figure is a grouping of 6 panels, where A-E visualise an increase in plasma levels of ctDNA in 5 individual patients, 1 patient per panel, as they were collected over time. The  $y$  axis shows variant allele frequency (VAF) of gene mutations that compose each “custom patient-specific



**Fig. 7.1** “Personalized profiling detects rising ctDNA ahead of clinical relapse”—diagram published in Coombes et al. (2019)

panel”, and these lines plot the number of variant reads divided by the number of total reads and reported as a percentage. The  $x$ -axis shows days after surgery. The lead time—the interval between ctDNA increasing in plasma samples to indicate recurrence and when the patient was diagnosed via the hospital’s existing screening system—is shown at the top of each panel by a red triangle and blue triangle connected by a dotted line and expressed in days. This is the time interval between clinical relapse (red triangle) and molecular relapse (blue triangle). In contemporary breast cancer care CA 15-3 biomarkers are routinely used to monitor for cancer relapse. This biomarker is also graphed here (teal circle), with baseline levels (32 U/mL) marked in light blue.

These diagrams are used as visual evidence and proof of a wider set of practices that call on figures in different ways—methods of analysing and valuing figures in the interests of accurately predicting change. They show how EBLIS figured cancer in time: according to the durational intervals significant to tracking ctDNA and to a process of figuration that makes this time known as an experimental object. As we observed the study, we also became aware of the different horizons of hope and expectation being tied to the study’s progress. As results emerged, patients were able to picture themselves in novel ways. However, while the research was being conducted in clinical contexts, the application of study outcomes were differently distributed. Interviews revealed the many interpersonal and institutional contexts by which practices of material and symbolic figuration were taking place, as well as the wider, consequential phases of clinical research that different stakeholders expect EBLIS to follow.

## Inhabiting Cancer’s Figures

Diagrams establish and maintain internal and external relations, drawing connections between multiple objects, practices, and persons. They contain common elements, according to what Sybille Krämer and Christina Ljunberg call “diagrammatic scenarios”—a synoptically flattened order or form spread across a two-dimensional plane, involving the interplay of points, lines, or surface points that articulate a set of homogenised relations. These elements ensure the diagram’s reproducibility as a schema.



Rather than genres of image that are self-referential, Krämer and Ljunberg ask that we consider the “alloreferential” capacity of diagrams, which signify many and multiple concepts and objects of knowledge external to their form (Krämer and Ljungberg 2016: 10-11).

The word ‘diagram’ has this connectivity stowed in its etymological history, deriving from the Greek *diagraphēin*—*dia-*, ‘across, through’, *graphein*, to ‘scratch,’ ‘carve,’ ‘write’; ‘to mark out by lines’. Modern diagrams function as “icons” that, according to Peirce, are used to gather “a set of rationally related objects” amenable to experimental practice and reason (Peirce 1976, 4: 316). And yet diagrammatic icons, for Peirce, do not relate objects passively or by neutral reason but take “the middle part of our reasonings”, as mediation (Peirce 1998, 5: 163; Bender and Marrinan 2010: 23-56). EBLIS represents an approach to determining cancer’s presence that is figural, insofar as it involves the presentation of knowledge mediated in diagrams. It invokes visual forms that picture relapse as a temporal phenomenon for individual patients. But as an experimental approach not yet fully tested and adopted into clinical practice, it is also temporary, provisional, and promissory, with regard to its truth and its future use. So, although the basis of likeness and comparison for current prognostic tools can draw frustrated confusion among users, the significance of EBLIS is that likeness and comparison are personalised, serialised as  $n=1$ . The objects they relate, the lines marked out mean they give a capacity to be inhabited and embodied (Haraway 1997: 11). This capacity, however, remains a promise at this stage of the research, it is prefigured, and these promises differ for patient-participants involved in the study as they do the clinicians and scientists leading the research, and the organisations, funders, and companies that participate in the study’s progress.

Figural representation in the tradition considered by Erich Auerbach (1938/1959) involves a first event or person signifying both itself and the second that it involves or fulfils. Serial and recursive forms of historical representation structure and authorise the anticipation of prospective potential and retrospective analyses. Past and future phenomena are at once articulated and entwine. As a historical and aesthetic framework, Auerbach’s theory of figuration illuminates the present as it is known and experienced as fulfilling a past, with each event or type of the past having

the potential to join another in the future. It is in this sense these figures depend on time lived conditionally, partially, or in state of waiting and abeyance. As historian Hayden White noted of Auerbach's figures, their flow and sense of trajectory is not known according to a linear sequence: "the making of a promise," White writes, "can be deduced retrospectively from a fulfilment, but a fulfilment cannot be inferred prospectively from the making of a promise" (White 1999: 89).

While Auerbach's historical theory concerned a combination of theological and literary examples, combining the material-symbolic fulfilment of parabolic narratives, signs, and portents. He theorised the distributed effects of figures as epistemic patterns and as ways of materialising the abstract, making the symbolic concrete in a moving present. The making of molecular relapse as a form of historical knowledge cannot (yet) be determined prospectively; it needs the retrospective relief of clinical relapse to have epistemic value, in the same way that biblical testaments are marked old and new in a figural relation to one another. While personalised blood monitoring of ctDNA presents a novel technological intervention based on high-throughput, next-generation genetic sequencing it also follows an archaic analytic structure, insofar as it relies on serial figurations of something unresolved: a (yet to be defined) disease-in-progress. Figures of this kind follow one and another, as figures prefigured, as each test depends and has value according to its place in a sequence.

As a study whose aim is to bring greater certainty over future events, the outcomes of EBLIS were uncertain when we were conducting our fieldwork. Given this uncertainty its figures needed to be managed for patient-participants, and they, in turn, needed to learn how to manage figures of promise. When enrolled into the study patient-participants were told that clinicians and researchers "will not be performing any tests that have an influence on your care. It is therefore unlikely that the study will yield any new information that will affect you personally."<sup>2</sup> As a consequence, study feedback to patient-participants was limited to communications concerning their continued participation and enrolment. Because clinical researchers were unsure of the outcomes of the study and

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<sup>2</sup> Patient Information Sheet (13/LO/1152), Version 4, 10/10/2018.

because there exists no data to show that treating patients based on ctDNA has better clinical outcomes, patient-participants in EBLIS could not follow ctDNA levels as they were being tracked by this research group. They occupied and were preoccupied by the figures but did not (yet) inhabit them.

When participants were recruited and when they were later consented to extend the study in 2018–2019 for a further 4 years, they were told “there is no benefit to you personally from taking part in this study.”<sup>3</sup> But visits to the clinic formed part of the research and gave patients access to an oncologist: a skilled specialist that understood and appreciated the potential long-term side effects of hormone medication that many participants were taking. The clinician who met them every six months felt the care she gave was minimal: “they are so stable, it’s quite a steady thing in the trial clinic just doing the same thing on them every six months. You’re not giving them anything, especially in the EBLIS trial, I’m not treating them, I’m not giving them any medicine”. But patients we spoke to perceived (and some reaped) the benefits of a greater level of care than if they were not research participants.

When we interviewed them almost all the women we met reported benefits that were psychological or material, personal, interpersonal, or social. Jill told us that she liked “the possibility to come here [to the hospital] every half year, even though my treatment is finished already”.<sup>4</sup> This gave her “peace of mind” and made her feel “more relaxed” about her cancer and its uncertain future. Likewise, Margret appreciated the sense that she was being monitored, not by the new technologies being pioneered by EBLIS researchers but by simply feeling that “someone was keeping an eye on me”. Gaining peace of mind in the present and near future, through the continuity of care that research participation offered was seen as one benefit. The benefits of liquid biopsies in the future were less clear.

These contrasts over the valuation of care in the research may indicate the differing interpretations of what being ‘stable’ means according to patients and clinicians, at different stages of cancer care, particularly in

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<sup>3</sup> Patient Information Sheet (13/LO/1152), Version 4, 10/10/2018.

<sup>4</sup> All names used are pseudonyms.

the precarious period after treatment when cancer may or may not recur. They are differences of perspective that pivot with the availability and distribution of clinical and experimental figures, that also mark a difference between ‘standardised’ provisions of care and those associated with research. Although participants were not able to inhabit the personalised figures that tracked ctDNA, they valued being monitored in trial clinics and believed that they would help bring improvements to clinical practice in years to come. Participating in this research study helped them manage the uncertain relations with their own health, while contributing to the transformation of relations to risk for others.

The promise-fulfilment structure characteristic of Auerbach’s description of figuration illuminates these shadows these developments in EBLIS and in the larger field of molecular genetics. Of the 13 women we interviewed in 2018–2019, 4 understood that EBLIS was tracking their ctDNA in a way that they understood to be ‘personalised’ or ‘individualised’, and in this sense they understood the broad intention of the specific research study. Many spoke in broader terms of tracking biomarkers in the blood, and this would, they assumed, help bring about a more timely diagnosis for other cancer patients. Comprehension of when this might be possible and how tended to be vague. One participant explained that she simply wasn’t sure whether the study was looking at “bits of DNA or bits of protein. I don't know what they were looking for”.

How the information EBLIS generated about patients and patient groups, and how study information may influence the course treatment, was also unclear to others. One woman was confused as to whether or not EBLIS would help her understand her risk of relapse. As the conversation developed she said she wanted to learn more about what was being discovered: “what are they finding out from it, because that’s interesting in itself” she said. “Even if they were finding out nothing, that would be quite interesting too, wouldn’t it?” Another woman expressed her frustration at not being told more about the research study she was involved in. Susan told me that she is eager to participate in research provided that participation meant the outcomes were transparent. She felt that an opportunity was being missed to think differently about the individual as a research participant: “you’re dealing with people and you want to make it individualised medicine,” she said, “so if you want to individualise it,

you can't ignore the individual.” And yet, as we found when we interviewed clinicians and researchers, returning experimental results with no proven or straightforward programme of treatment could risk a duty of care involving clinical, ethical, and legal promises that cannot currently be fulfilled.

Wider contributions from social science and humanities scholars have noted the harms of elevated or unrealistic promises and expectations associated with more personalised or precise medical approaches (see Feiler et al. 2017; Erikainen and Chan 2019). These scholars stress the shortfalls between promise and reality and the personal and public losses that follow (see Dickenson 2011; Prasad 2016; Maughan 2017; Rushford and Greenhalgh 2020). Others have documented how hype, promise, and expectation play a constitutive role in biotechnological innovation, with discursive speculation influencing the material shape, quality, and extent of collaborations, resource allocation, and markets (e.g., Brown and Michael 2003; Brown and Michael 2003; Martin et al. 2008; Adams, Murphy, and Clarke 2009; Tutton 2012; Haase et al. 2015). These sociologies of expectation, hope, and anticipation document the work of discursive prospecting that accompanies biotechnological innovation. Research in liquid biopsies coordinates and manages resources via an iterative, test-retest logic of embedded promises and expectations. And studies like EBLIS, with its graphic recomposition of text, image, and number, and its provisional stratification of persons according to molecular progression, do not pose one possible future but many.

In addition to the views of patient-participants, whose hopes and expectations we found to be managed within a framework of rolling consent common in translational research, our interviews with clinical and laboratory researchers managing EBLIS saw its potential in different ways; they recognised its accomplishments, uncertainties, and possibilities, figuring different durations via given modes of participation. Currently, patients receiving cytotoxic therapies for overt metastatic disease rarely see curative outcomes. In the more distant future, with an expansion of trials and studies that can investigate using ctDNA levels to guide clinical decision-making, it might be possible to “salvage patients who are ctDNA-positive with second-line therapies” (Coombes et al. 2019). Here there is a desire for a just-in-time change to future outcomes,

based on better predictions of what is likely to pass. One clinical researcher, interviewed at the time the article in *Clinical Cancer Research* went to press, described EBLIS as being able to “open the door to potentially an entirely new paradigm“ for diagnosis, treatment, and monitoring.

This clinical interest in treating patients earlier and providing them with better clinical outcomes was contrasted to the potential problems this technology might cause in the more immediate future:

we’ve developed a test which is in advance of having any treatment for the patients, which has been proven to benefit them. So in a way, from the patients’ point of view, I think it’s a bit of a disaster, because now it’s going to be wheeled in, these results are all going to be given to all the patients. They’re going to have their results that show they’ve got some problem in the blood, and then they’re going to come back three months later and it’s going to be even higher. There’s going to be no scan evidence of any disease, and the doctors won’t know what to do.

At a stage when the patient using liquid biopsies in this breast cancer clinic remains a figure to be realised—at least in the NHS—the treatment of patients remains dependent on future programmes of research that enter further, iterative patterns of promise and fulfilment.<sup>5</sup> In this clinician’s view EBLIS indicates the need to follow stratified sub-groups of relapsed patients whose earlier treatment could show the benefit of treating at the point of molecular rather than clinical relapse:

at the point of molecular relapse, you could have a total of perhaps as many as 10 to 20 phenotypes of patient. So you’re going to have to design multiple trials for each of those subcategories of molecular relapse, each of which will involve as many as 1,000 patients, and long follow up, and survival analysis.

Previous patient cohorts that were divided and treated by broad molecular and histopathological groups may now face further subdivision, according to when and how they relapse via threshold numbers of ctDNA

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<sup>5</sup>At the time of writing this chapter, liquid biopsies were being trialled in different NHS sites (see NHS England 2020).

detected. What is distinctive for the personalised tracking of cancer when thought in terms of its promissory structure then is not that it is subject to a see-saw motion of hype and disappointment, or that it makes a single promise for a group of susceptible patients and investors, but that the system of analysis redistributes the basis of clinical groupings and the temporal grounds that once grounded predictions over long- and short-term durations. Historical time for individuals and groups is reconfigured with molecular evolution. Through a logic of serial testing and retesting, EBLIS marks out in lines the course of disease for individual patients, while recalibrating how cancer patients compare (or no longer compare) to others.

The graphic compositions noted above relate and visualise movement in forking, braiding deltas, where lines are read as figures not only of changing biomarkers that indicate somatic change but also interpersonal and comparative figures of analysis and feeling, which mark out links within and between individual patient-participants, as well as the wider ecologies of contemporary translational research in the biosciences (see Crabu 2018; Rajan and Leonelli 2013). Figuration links and combines via various scales, sources, and kinds of data, at once intimately personal and radically impersonal in terms of both duration and bureaucracy.

Studies such as EBLIS figure cancer's progression in experimental periods or intervals. These are significant for individuals in that they may influence the categories of disease status that help guide clinical decision-making. They may affect more generalisable definitions of precision by adjusting the 'right person' at the 'right time' with the 'right treatment'. In this sense, rather than simply fulfilling existing hopes and expectations attached to fixed ideas of 'precision' or 'personalised medicine', EBLIS refigures the temporality of the personal and the precise. However, even within the relatively short time period that EBLIS has been active, a study punctuated by documenting the utility of ctDNA for tracking breast cancer patients at high levels of patient specificity, it does not maintain a fixed understanding of the right person or the right time.

The first phase of research showed the non-invasive detection of pre-clinical metastases using a personalised ctDNA analysis. Researchers used tumour exome data to design patient-specific 16-plex assays and deep sequencing of plasma cfDNA at an average depth of 100,000 reads per

target, a sensitivity to the level of a single, mutant molecule. The next phase of research involved extracting the whole-exome sequencing (WES) data from serial plasma samples to find novel mutations and new copy-number events that evolved from the primary tumour (see Hastings et al. 2021). “You can also track the evolution of the tumour,” explained one bioinformaticist, “and you can also see if a patient is responding to treatment or not.” While the clinical researcher focussed on the validation of liquid biopsies in different patients, their colleague highlighted a potential for further research to understand the specific molecular characteristics of each relapse. Since blood samples taken from EBLIS participants were relatively large in volume, researchers explained that this next phase would use the same samples and occupy the same time points. In this sense the first phase of EBLIS could serve figures that then contrast to experimental figures of the future, where the first iteration informs the next. As serial test EBLIS has a serial, test-retest relation to its own progress. This additional layer of potential in the study data, working in parallel to patient-level tracking in follow up, and WES tracking of progression and monitoring among metastatic patients, promises a prognostic tool. The excitement that accompanies developments in molecular oncology may not necessarily lead to an infinitely granular segregation of cancer categories, treatments, and predicted outcomes, but to their recombination, albeit made up of different figures and a different idea of portraiture.

In short, EBLIS has multiple horizons composed of overlapping parts. These compositions and contrasts are a work of figures used to present its data; a broader, interlocking programme that progresses by incremental phases. Indeed, in combination with EBLIS phases one and two is another; there is a further phase of research that is broadly biostatistical and predictive in nature, aiming to take clinical and genomic data from other EBLIS sub-projects to build a prediction model using machine learning techniques. This model would “apply to anybody who’s coming into the study, or any cancer that gets sequenced. You could run it against this model and see if they fit the criteria of a patient who might relapse”. At the time of our interviews, using the data of relapsed patients to create a predictive model was in an early phase of planning and development. But even as a hope or possibility it tells us how a personalised,  $n=1$



tracking study could be used to build different kinds of prospective cohorts—data to build a prognostic tool to determine another set of standardised outcomes.

## Conclusion

In her 2019 memoir *The Undying*, Anne Boyer describes her diagnosis and treatment history. “My tumour,” she writes, “started on a screen, and I returned it there. I entered its precise qualities into the prognostic calculator that promised to display the future in a pictograph. The dead women were represented by forty-eight dark pink frowning faces, the living ones by fifty-two smiling green ones. All of these faces were supposed to, like me, be forty-one years old and with exactly the same version of my disease, but none of these faces, living or dead, said why or when or who” (Boyer 2019: 41-42). Boyer explains that her disease is known to her as a screen image and her tumour’s mediated qualities are not exclusively biological, they extended across a vast and comparative network. The sensory status of cancer as a ‘silent killer’ has long been linked to its malignant and unpredictable danger, giving further reason to picture it in different numbers, images, and texts. Personifying cancer’s evasiveness—as a figure difficult to see, hear, or touch—is closely linked to cancer’s exposure, capture, and control (Sontag 1978; Bowker & Star 1999; Lochlann Jain 2013; Semino et al. 2018).

This chapter has explored how novel molecular figurations of breast cancer challenge established methods of picturing its future course, both by breaking up sub-groups and by allowing the rapid introduction of targeted therapies. Meanwhile, research in the field of ‘liquid biopsies’ generates ways of figuring disease recurrence that tracks changes in disease for individuals, as a line or path determined by combinations of data. What this chapter has been keen to stress is how the workings of EBLIS for individual patients involve a *layering* of figures, emerging and residual, novel and archaic in pattern, that parallel trajectories of development and progression integral to wider infrastructures of translational research. To what extent such figures can be symbolically and materially

inhabited is a question of time. Or rather, a question of how time is questioned, coded and tracked, transformed into protocol and standardised.

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