Promising precision medicine: how patients, clinicians and caregivers work to realize the potential of genomics-informed cancer care

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This paper examines the emerging field of molecular oncology, in which targeted treatments are sought for patients who have exhausted standard cancer therapies. Drawing on an ethnographic study at a U.S. academic medical center, and building on recent theoretical work examining potentiality as a site where expectations, meaning and value are produced, I describe efforts to translate genetic information into extended life for patients. Clinicians, patients and families performed various types of largely-unrecognized labor that invested precision medicine with potential even when life-prolonging therapies remained elusive. Their future-making work was enabled and constrained by the structural conditions of U.S. health care. In this context potentiality was a generative force that was harnessed to the interests and inequities of a market-driven health system, raising important questions about who is able to participate in, contribute to, and benefit from emerging innovations and narratives of hope.

Keywords: precision medicine; potentiality; cancer; genomics; equity

Introduction

In 2015 President Obama announced the U.S. Precision Medicine Initiative and the coming of a “new era of medicine” (White House 2015; Ashley 2015). Invoking a “curable future” (Gibbon 2013), the president anticipated that before long medicine will be able to deliver “the right treatments, at the right time, every time to the right person” (White House 2015). The forward-looking promise of precision medicine, also referred to as “personalized medicine,”¹ is being propelled by large-scale public initiatives including the U.S. All of Us Research Program and the UK Biobank, as well as public-private initiatives such as the European Union’s Innovative Medicines Initiative. The promissory statements and images put forth by these programs are shaping public expectations, and, by

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continually re-invoking the potential of precision/personalized medicine, they also provide a rationale for funding and building large research and clinical enterprises.

This paper examines the concept of potentiality as it relates to the use of genomic technologies to inform cancer treatment after standard therapies have been exhausted. In their introduction to the 2013 special issue of *Current Anthropology*, Karen-Sue Taussig and coauthors describe potentiality as a central concept in the life sciences and biomedicine—a “hopeful idiom” used to invoke the expected benefits of new medical interventions (Taussig, Hoeyer, and Helmreich 2013). They point out that potentiality is rarely explained or analyzed, perhaps because it is so deeply and unconsciously woven into the fabric of scientific and public discourse, and perhaps because it is complex and difficult to get a handle on, since thinking or talking about potential is to invoke something that does not (yet) exist and may never exist. Although potentiality is a concept linking hope with imagined futures, investments in the promise of biomedical futures have real political and material consequences in the here and now. In her work on scientific efforts to understand children’s cognitive and emotional differences, for example, Rayna Rapp demonstrates the productivity of invoking potential for amassing funding and developing new tools, and how, even when unsuccessful, these tools can be folded into newly imagined futures (Rapp 2011). In other words, “potentiality is disconnected from what may actually happen but paves the way for desirable futures” (Timmermans and Buchbinder 2013, S27).

Recent explorations of the biosciences from within science and technology studies also engage with the concept of potentiality and the generative power of expectations. The sociology of expectations, for example, explores how anticipatory rhetorics prompt resource mobilization, technological innovation and scientific activity and are made material by becoming embodied in objects, actions, and bodies (Borup et al. 2006). Emphasizing the “situatedness” of future-oriented discourses, Brown and Michael (2003) detail how these discourses shape and are shaped by actors’ positions and the networks in which they operate. Anthropological investigations of the future orientation of biomedicine, meanwhile, include Adams, Murphy, and Clarke’s (2009) examination of the concept of “anticipation” as an affective state that is both felt, lived and shared—a “moral economy in which the future sets the conditions of possibility for action in the present …” (249).

Oncology is in the vanguard of efforts to make good on the potential of precision medicine, with emerging research-clinical collectives using genetic sequencing to improve diagnostic accuracy, predict responses to therapeutics, and match patients with clinical trials of experimental treatments that “target” specific molecular pathways. Unlike other domains of genomic medicine, which focus on identifying the etiology of suspected genetic conditions and managing future risk, molecular oncology is occupied primarily with the present through predicting the connections between genetic mutations and drugs and devising new treatments based on these hypotheses. The treatment plans emerging from molecular analysis often involve the use of experimental drugs, which can be difficult to obtain and
may require enrollment in a clinical trial, for which a particular molecular profile can be a prerequisite. Thus, clinicians and patients find themselves seeking new therapeutic options in the midst of “increasingly dense connections between genomics research, cancer care, and the clinical trials system.” (Nelson, Keating, and Cambrosio 2013, 424).

As genomics research, therapeutic innovation, and cancer care become more interdependent, the meanings and practices encompassed by the terms “research” and “care” in oncology are less clearly delineated. Keating, Cambrosio, and Nelson (2016, 32) argue that oncology’s embrace of translational research has provided the conditions in which research and care have become more entangled, such that “clinical interventions in the age of targeted therapy are simultaneously explorations of the molecular mechanisms of normal and pathological cellular processes.” Genomics has become a key site in oncology and other medical fields where the distinction between research and clinical care has blurred (Wolf, Burke, and Koenig 2015). The mutual reshaping of research and care is instantiated in the body of the patient, who “becomes simultaneously a locus of experimentation and the subject of hopefully more effective (because more precisely tailored) care” (Cambrosio et al. 2018, 217–218). Located at this blurred research-clinical care boundary, molecular oncology and other precision medicine efforts depend on patients’ contributions of data and biospecimens and on other “ethically complex and controversial research modes such as biobanking and data mining of electronic health records” (Erikainen and Chan 2019, 320).

Empirical studies of molecular oncology have focused on emerging “bioclinical collectives” which have upended the traditional division of labor between clinicians and biologists as well as troubling the practical and conceptual distinctions between research and clinical care (Bourret 2005). The hallmark bioclinical collective in molecular oncology is the molecular tumor board, whose multi-disciplinary members interpret genetic information, make diagnostic and therapeutic recommendations, and guide patients to appropriate clinical trials. Other collectives involved in re-negotiating the research-clinical distinction in molecular oncology include genomic databases and algorithms that serve as both research tools and guides for routine clinical treatment decisions (Cambrosio et al. 2018).

There has been less research on the work that patients, clinicians and caregivers contribute to building the emerging field of molecular oncology. Exceptions include Kerr and Cunningham-Burley (2015), who document how participation in clinical trials has become an established aspect of cancer care for growing numbers of patients. They demonstrate that being a cancer patient now involves various types of “embodied or emotional work” that go beyond the expected donation of tissue and data to include traveling long distances to participate in clinical trials, cultivating relationships with clinicians, and performing narratives of “hope, sacrifice and participation” (Kerr and Cunningham-Burley 2015, 192). Although patients’ work has been largely unrecognized, they argue that it is essential to projects of biomedical innovation. Another example is Brown and de Graaf
(2013)’s study of patients with advanced cancer participating in drug trials, who work to construct and manage multiple possible “future-times.” These cognitive and emotional labors enabled hopefulness in the midst of uncertainty and poor prognoses.

Drawing on an ethnographic study at a U.S. academic medical center, this paper extends the literature on the largely-unrecognized labors of patients and clinicians who are involved in efforts to translate genetic information into life-extending cancer treatments. I focus on genetic tumor profiling for patients with late-stage cancer, which is situated at the intersection of clinical care and research. To explore practices and narratives related to molecular testing for advanced cancer after standard treatment options had been exhausted, I followed patients, clinicians, and family caregivers through the testing process and its aftermath, documenting routine, local practices such as deciding whether to recommend and undergo genetic testing, considering the cost of the test, contributing biospecimens, identifying and procuring experimental treatments, and managing disappointment.

Below, I describe the everyday work of genomic medicine that Kerr et al. have characterized as invisible and undervalued but also “…crucial to the test, treatment or research being conducted, and thereby closely linked to the work of crafting a future for ourselves and others” (2021, 8–9; see also Swallow et al. 2021). In the U.S. context, the work of cultivating hope, tempering expectations, managing tissue, and procuring experimental treatments is enabled and constrained by a vast clinical trials industry, the labyrinthine financial and regulatory structures of U.S. healthcare, and entrenched inequalities in access to care. I consider how efforts to realize the potential of genomic medicine sustain affective and material investment in an imagined future while simultaneously (re)constituting a bioeconomy with stratified possibilities for participation, hope and benefit.

**Methods and setting**

This paper is based on fieldwork conducted at a large U.S. academic medical center shortly after the launch of a clinical test called a “cancer gene panel.” The test involved genomic sequencing of hundreds of genes associated with cancer in order to compare changes in “somatic DNA” in a patient’s tumor tissue and “germline DNA” in a blood sample. These changes, often referred to as alterations or mutations, were used to identify therapies targeting particular molecular pathways, match patients with clinical trials, and improve diagnostic accuracy. The panel was ordered primarily for patients with incurable cancer who were no longer responding to standard therapy, and for whom experimental therapies were the only remaining option for life-extending treatment.

The gene panel had been developed and launched with financial support from the medical center, meaning that clinicians had initially been able to order the panel for a patient without worrying about cost or insurance coverage. At the
time of our study, however, startup funding had expired, with the medical center expecting the test to transition from a subsidized, largely-experimental endeavor to a revenue-generating service. Billing health insurers for the cost of the test was underway, but it was uncertain whether insurers would agree to reimburse the cost of the test due to a lack of robust evidence of benefit. Therefore, it was possible that some patients would be expected to pay the medical center for the cost of the test, particularly those without insurance or with publicly-funded insurance, which provides more limited coverage for genetic testing than private insurers.

Over the course of a year, a graduate student and I observed weekly meetings of the institution’s “molecular tumor board,” which convened clinicians, pathologists, molecular biologists, bioinformaticians, and genetic counselors to discuss gene panel cases. Tumor board discussions focused primarily on interpretations of identified “pathogenic” variants and possible targeted treatments indicated by them. Germline findings were rare, but when they arose the board discussed cancer risk implications for the patient and their family members. We were particularly interested in observing how the cases of patients whom we interviewed were discussed (some were not because no targetable mutations were identified), including interpretations of genetic variants’ actionability and therapeutic and clinical trials recommendations.

We also conducted interviews with oncologists (9), a molecular biologist, patients (12), and family caregivers (7). We were able to meet with two of the 12 patients at two times points: before receiving their genetic test results and several weeks afterwards. Interviews lasted 60–90 minutes and focused on the patient’s treatment journey, decisions about genetic testing, understandings and expectations of molecular oncology and precision medicine, interpretations of test results, attempts to procure experimental treatments, and expectations for the future. Four of the 12 patients permitted me to observe clinical sessions in which genetic test results were discussed with an oncologist. We did not encounter or speak with cancer patients who had opted out of molecular testing. Although it is likely that refusals occurred, we did not learn of them. Nor did we encounter patients who might have been eligible but were not able to undergo testing for health, financial or logistical reasons. Given the high costs of medical services and lower reimbursement rates set by publicly-funded insurance agencies, including Medicare and Medicaid, access to specialists is limited among lower-income patients in the U.S. Therefore, patients who were unable pay the out-of-pocket costs of medical services, or travel to the medical center, largely remained outside of the promises, hopes, disappointments, and collective labors of molecular oncology at the academic medical center. It is important to acknowledge that their voices are missing from this account.

All interviews and clinical sessions were audio-recorded and transcribed. The study received ethics approval from the academic medical center’s institutional review board (approval number 16-19731). Participants were given a document
with information about the study and thereafter were asked to provide verbal consent to participate. The names used throughout this article are pseudonyms. I conducted all observations and most interviews, and several interviews were conducted collaboratively with the graduate student researcher, therefore the text alternates between “we” and “I” when reporting from the perspective of the researcher(s). My process of interpreting the future-looking narratives and practices of study participants was based on the “constant comparative” approach, in which interpretations are made and revised as each new account is considered (Corbin and Strauss 2014). The themes I report below are those that were predominant in clinic observations and interviews, with tumor board observations providing an additional source of insight into how expectations of the future shaped clinicians’ decisions about treatment and clinical trials options for their patients.

As mentioned previously, the comparison of tumor and germline DNA sometimes resulted in the identification of inherited alterations with cancer risk implications for the patient and their family members. The distinctly different uncertainties and ethical challenges facing clinicians and patients in considering germline and tumor alterations meant that oncologists and patients were compelled to alternate between what Bogicevic et al. (2020) refer to as “the germline mode” and “the somatic mode” of care. In the germline mode, which has been predominant since genetic testing was developed, genetic information is conceived and acted on as personal information about an individual and their biological kin. Emphasizing risk prediction and disease prevention, the germline mode tends to be future-oriented. The somatic mode, by contrast, is focused on the present and conceptualizes tumor DNA as a biological resource that is separate from the patient as a person - much like cancer is conceived as foreign and non-self in oncology. In the somatic mode, “‘doing good’ is to attend to the present cancer and patient, and search for possible therapeutic pathways” (Bogicevic et al. 2020, 16).

The distinction between these two modes is more blurred in practice: genetic information is never fully disconnected from heredity and notions of the person, and the somatic mode involves anticipating patients’ possible futures while caring for them in the present. Nonetheless, in this article I lean toward the somatic mode, focusing specifically on efforts to create hope and therapeutic benefit from genetic information in a patient’s cancer tissue and touching on germline information only when it has a bearing on the practices and narratives surrounding tumor profiling.

In what follows I examine the largely-unrecognized work that clinicians, cancer patients and caregivers performed in an effort to realize the potential of genomic medicine. I consider three types of labor: the first is the construction of possible futures and the ways in which “future thinking” (Jain and Kaufman 2011) combines with present realities of prognosis and health insurance coverage to constitute what can be imagined, hoped for and accomplished; the second is the effort to manage and conserve human biopsy tissue as a material embodiment of the
potential of precision medicine; and the third is the collaborative work of transforming genetic information’s potential into extended life. A thread running through these three discussions is the role of potentiality as a generative force that is harnessed to the demands and inequities of a market-driven health system, raising important questions about who is able to participate in, contribute to, and benefit from emerging innovations and narratives of hope.

**Anticipating potential futures**

In this section I consider several forms of anticipatory work in which the potential benefits of genomic medicine are weighed against concerns about the affordability of testing and patients’ limited time horizons. Future-oriented narratives and practices helped to buoy patients’ hope and propel the genomic medicine enterprise, while being shaped by structural conditions that allocate potential and limit participation.

**Recommending genetic testing**

Oncologists usually recommended tumor DNA testing when standard therapies were no longer proving effective for a patient. An oncologist explained that the hope was to find “molecular features that we can target with drugs” and that “would have the potential of prolonging their life potentially or at least help dealing with symptoms and stop progression.” In considering whether to recommend genetic testing to their patients, timing was crucial and, for clinicians, morally-inflected. They particularly wanted to avoid the unfortunate possibility that test results would be returned too late to help a patient. When contemplating whether to recommend testing they weighed how much time the patient might have left to live against the potential benefits of genetic information for the individual and their family. On the one hand, testing can open doors to promising clinical trials and experimental therapies, and can potentially reveal inherited variants with cancer risk implications for family members. On the other hand, procuring investigational drugs can be an arduous process that is fraught with uncertainty. Even when targeted treatments are available, their therapeutic effects may be short-lived and side effects can be difficult to live with. At the time of our study only a small proportion of patients undergoing genetic testing were eventually matched with targeted treatments. “…on average it is just a few percent of people who get some tangible benefit from this in terms of their anti-cancer therapy,” reflected an oncologist. Enrolling in a clinical trial or waiting for approval for investigational use of a drug is not a good way to spend the final months or weeks of one’s life, this clinician and others reasoned. The same oncologist described the moral dilemma he found himself in when considering genetic information as both a source of hope and a possible harm by way of false hope or suffering caused by futile treatment:
There is this weird tension of like wanting to help the patient, treat the cancer but also make sure that if they are dying that they are dying in the best way that is possible. There is a lot of tension there if they are really sick. I try and send this [gene panel] in patients who are fairly healthy.

This quote highlights the ambivalence of the potentiality assigned to genomic medicine. On the one hand is the possibility that medical innovation can extend patients’ lives, which is welcomed by clinicians and patients. On the other hand is “ordinary medicine’s” shift to the use of life-prolonging therapies at all costs, creating quandaries for patients, families and clinicians as they face decisions about “when, where, and how to draw the line” (Kaufman 2015, 2).

Another preoccupation was testing too soon. A physician who played a key role in the molecular tumor board explained that genetic information should be used to identify experimental treatments only after standard therapeutic options had been exhausted. Nevertheless, he said, the test is sometimes ordered preemptively for patients at an earlier disease stage, motivated by clinicians’ fear that they would have nothing to offer the patient if the disease returned, as well as by enterprising patients who leverage social connections to request genetic testing in the hopes of securing more “personalized” treatment early in the course of their illness:

There is also a subset of patients who specifically come in asking for genetic panel testing of their tumor, frequently because they have a family friend who is a physician who is saying, “You have to get this because they are going to find a drug that is going to be the answer.” And I am going through and explaining that the odds of that are relatively low but, yes, we can certainly do this.

In considering early genetic testing for patients still undergoing standard treatment, oncologists acknowledged that it was unlikely to help the patient in the short term but reasoned that a molecular profile could serve as an investment in the patient’s therapeutic future: “let’s save it and we can continue to revisit it,” a physician recalled telling patients. A patient explained her experience with an oncologist who took this approach:

What [the doctor] said was, “It doesn’t change what we are doing now,” which is a six-month [chemotherapy] treatment, but that it might be something to know about in the future in case there is any metastases or if this is not effective for some reason. […] We knew that Dr. C was good at this, that it was one of his specialties to do genetic thinking, the most up-to date thinking, which made us very happy.

These narratives indicate that for a subset of enterprising patients, tumor genetic testing had become an essential component of individualized cancer care – a means of banking on precision medicine’s potential. Genetic information was unlikely to lead to treatment changes for these patients for the foreseeable future. Its value, rather, was as an early investment in a future that was expected to bring rapid developments in genetic knowledge and an expanding menu of targeted cancer treatments. Moreover, obtaining a molecular profile enabled clinicians and patients to participate in personalized medicine as a “promissory bioeconomy”
whose narratives and activities are premised on the fostering of hope through “local networks of non-monetary exchange, trust, personal care and obligation” (Haase, Michie, and Skinner 2015, 2). Even in the absence of therapeutic benefit, said an oncologist, “… it makes them feel that their care has been more holistic and complete and tailored to them.”

We learned that not all molecular tumor board members shared this perspective, and at least one clinician told us that testing at this stage was rarely appropriate and that, moreover, discussing the results of tumor sequencing for patients with early stage cancer was not a good use of board members’ time. However, clinicians’ willingness to conduct state of the art genetic testing for patients who have not exhausted standard treatment options reflects a biomedical culture in which saying no to innovative therapies and tools “seems like refusing to take the path of progress” (Kaufman 2015, 14; see also Kaufman 2013). At the same time, most cancer patients in the U.S. do not have trusted relationships with oncologists at top-tier academic medical centers, raising questions about who is able to make an investment in individual and collective futures through genomics and who is excluded from narratives of hope and practices of future making.

**Weighing the costs of testing**

Clinicians typically strive to separate diagnostic and treatment decisions from financial considerations, yet oncologists told us that they were morally obliged to weigh whether their patients could afford to pay for genomic sequencing given ongoing uncertainties about insurance coverage. Since genetic information was unlikely to directly benefit patients at this early stage in molecular oncology, being billed for sequencing was like being asked to pay to participate in medical research. An oncologist told us:

> I think it is hard enough for patients to come here, park in the parking lot, drive from [cities hundreds of miles from the medical center]. It is hard enough for them to do that and then to ask them to fork out $1500 for predominantly academic information is a tough pill to swallow …

To avoid surprising patients with an invoice for the cost of the test, some oncologists recommended a tumor-only gene panel from an independent laboratory that was known to waive the cost for patients lacking insurance coverage. Molecular tumor board members agreed that the information produced by the tumor-only test was less clinically useful than the paired tumor-germline information generated by the in-house gene panel. Indeed, efforts to interpret test results and identify treatment options at board meetings were sometimes stymied by a lack of germline information in a lab report. Nevertheless, in weighing cost and quality many clinicians and division chiefs leaned toward the former, extending the scope of care beyond the patient’s physical well being to encompass the economic consequences of participating in genomic
medicine. These considerations suggest that U.S. healthcare financing, including insurers’ reimbursement and coverage decisions, shaped the kinds of knowledge that could be created and made available to clinicians and patients and the ways that this knowledge could be used to help patients.

Managing uncertainty about the future

The patients and caregivers we spoke with were living with profound uncertainty about the future. Genomics-informed cancer care offered the hope of promising experimental treatments and extended time horizons, but was also understood to be an innovation-in-development. For patients with late-stage cancer, a crucial concern was the extent to which their own biographical future would intersect with the anticipated future of precision medicine. Would alterations in a patient’s tumor DNA point to existing targeted treatments — whether via prescription or clinical trial enrollment — in the near term or would the variants remain inscrutable to clinicians during the patient’s remaining months or years? To better gauge their chances, some patients dedicated time and effort to understand the emerging field of molecular oncology.

For example, I meet with an elderly patient, John, and his wife at the hospital’s “infusion center” where John is receiving chemotherapy for metastatic cancer. He explains that he feels tired and weak most of the time these days and apologizes in advance for dozing off occasionally during our conversation. John agreed to undergo genetic testing at the recommendation of his oncologist. While waiting for the results, he looked through scientific journals to educate himself about cancer genomics. He and his wife, Margaret, share their views about participating in genetic testing while facing a poor prognosis:

John: If they find something that is targetable and they have a drug that can attack it that is great. [...] I suspect the chances are small. We thought that the more information they have, the better off I will be. [...] I think in five years things will be much more productive in following this route of investigation. They will have better technology to get the material. They will know more about driver genes in cancer.

Margaret: You cannot go wrong with more information. [...] I think that the doctors are very much on the breaking edge of new things [...] I think that is exciting. A lot of people would like maybe the comfort of going to somebody who says, “Well, there is nothing we can do,” and just go home. But I guess that is not us.

John knows that he is unlikely to live another five years, yet his uncertain future is infused with possibility by being linked with the anticipated future of molecular oncology. He and Margaret find solace in participating in technoscientific innovations that bring precision medicine ever closer to fruition. Like John, other patients we talked with conceived of genetic testing as a predominantly experimental project and they were willing to contribute their
biospecimens and data to this population-level effort even with a low likelihood of personal benefit. Radhi, a woman in her 70s from a family of doctors and medical researchers, told us that she wanted to contribute to scientific progress: “I am interested in anything that could further the medical research, the medical science on my situation even if it is not going to have a direct positive effect on me …” On the other hand, some patients imagined precision oncology as a strategy for “buying time.” Even if targeted treatments do not deliver a hoped-for remission, they might possibly extend life until individual biography catches up with anticipated innovations in the future: “I know there are people working on stuff and that is kind of what I hope, that it buys me like five or ten years then in five or ten years there is something better,” said a patient. Genomic medicine’s potentiality thereby enabled conceptions of patients’ futures as open – a “time without horizons” – rather than foreclosed by disease (Del Vecchio Good et al. 1994, 856).

Clinicians’ narratives also tacked between an acknowledgement that genetic information was unlikely to change most patients’ therapeutic prospects and anticipation of future innovations propelled by patient data. An oncologist articulated the ambivalence of genomic medicine’s potential at this blurred research-clinical care boundary:

As a research institution, as opposed to a clinical tool, it would be nice to have more clinical data based on the tumor even at the outset for many people just as a research tool among other things. I still think it is reasonable to do it [genetic sequencing]. But in terms of how much it actually guides therapy it is the minority of people where you get something useful.

Although clinicians expressed unease with a test being considered “clinical” when its benefits to a patient are outweighed by the scientific potential of the data it is amassing, invoking the future promise of precision medicine helped them to manage their own disappointment when genetic testing came up short – and when the entire project of precision medicine seemed overly ambitious in light of the growing realization that “every patient’s tumor is different.” Over and over, clinicians invoked potential as the defining idiom of genomics-informed cancer care: “This is the first foot in the door into the whole realm of precision medicine,” said an oncologist.

Thus, clinicians who participated in genomic medicine conceived of genetic sequencing both as an investment in the future of precision medicine – by way of aggregating patients’ genetic information – and as a clinical tool used to help care for patients in the present. Gardner, Samuel, and Williams (2015, 19) call this effort “recalibration,” or the ability to manage “the tension between hyped portrayals of a biomedical intervention and the exigencies of clinical practice” (see also Kerr et al. 2019). The continual interplay of these narratives enabled both clinicians and patients to push forward, with everyday clinical activities infused with potentiality.
Conserving biopsy tissue as embodied potential

In descriptions of the emergence of genomic medicine in cancer care, genetic testing is often described as the conduit through which patients are able to access novel therapies, since these therapies target specific DNA alterations occurring in cancer cells. Tumor genetic testing is not possible without biopsy tissue, however, and cancer clinical trials often require a new biopsy or access to archived tissue. It can be argued, then, that the biopsy “comes to stand as the central gatekeeper for receiving targeted therapy” (Bogicevic et al. 2020, 14). Here, I consider biopsy tissue as a materialization of the potential of genomic medicine, and I explore how this potential is maintained through the work of procuring and managing tissue.

Obtained through a variety of invasive procedures, biopsy tissue is usually limited in quantity and variable in quality and consistency. It is in high demand in cancer research and care. “Every time somebody out there in the world wants to screen you, it consumes that material,” a patient told us. Patients and clinicians described becoming de facto managers of this scarce resource, grappling with existential dilemmas when deciding whether to conduct a biopsy or how to use archived biopsy tissue. An oncologist explained how she discusses tissue management with her brain cancer patients, whose excised tumor cells are particularly valuable because re-biopsy is often highly risky or not possible:

… more and more the pathologists are recommending [genetic] testing because that is limiting the number of tests that they have to run on the tissue and you can get most of the answers all once. That has been very helpful. I think the flip side is if you really do not have that much tissue and you are not going to act on any of the information that you are going to gain then a lot of the clinical trials that we have require you to send tissue, have archival tissue. If you waste that tissue then you are potentially eliminating options in the future from clinical trials for patients because you have used up all their tissue.

The tradeoff facing this clinician and her patients, then, is between using biopsy tissue to generate a genetic profile of the tumor, which could potentially point to a targeted treatment, or preserving the tissue in anticipation of future clinical trials, which could provide access to emerging investigational treatments. To further complicate this weighing of various possible time horizons, some clinical trials waive the tissue sample requirement if tumor genetic information is already available. “You have to decide how to use your limited tissue,” a patient told us, indicating that considerable knowledge and effort are required to become an informed custodian of a material that embodies both disease and the possibility of a cure.

The custodial work of tissue management is collaborative and embedded in trusting relationships between patients and clinicians. It also requires knowledge, not only of the complex clinical trial landscape and the latest scientific knowledge in cancer genomics, but also of government regulations and pharmaceutical
companies’ policies governing access to experimental drugs. Not all oncologists were able to stay abreast of these developments. In telling us that they had the best clinicians on their “team,” patients indicated an awareness of their privileged access to elite physicians. The teamwork metaphor also highlights the ties of reciprocal obligation among patients, clinicians and family members, which prompted clinicians to advocate for patients’ interests in sometimes contentious interactions with insurance and pharmaceutical companies dispensing and with holding investigational drugs. Even when all of these resources were in place, however, the lack of coordination among institutions that is characteristic of U.S. healthcare could limit the potential of biopsy tissue. This is illustrated in the story of a patient who was compelled to undergo an invasive procedure because his tissue had been discarded by another hospital:

They were going to get my sample of my tumor from [hospital in a different city] where I was operated … Anyway, Dr. Lee was all upset - I guess he contacted them and they discarded the tumor. By state law or something they are only required to keep it for five years but he was saying most hospitals keep it for ten … so I ended up having to have a core biopsy.

The lack of integration among U.S. healthcare institutions puts the burden of tissue tracking and transfer on clinicians and patients. Many patients obtain care at multiple institutions, change health insurance frequently, or do not have a trusted clinician willing or able to devote time to managing health information and tissue across institutions. For these patients, the potential of biopsy tissue may be diminished.

**Realizing potential futures by making genetic information “actionable”**

For most patients, genetic testing produces information that is of uncertain clinical significance and does not lead to changes in treatment. For some, however, a potentially “actionable” genetic alteration is identified, holding out the promise of an experimental treatment. In this section, I consider how clinicians, patients, and caregivers understand and respond to actionable genetic variants in a patient’s tumor tissue. I argue that genetic information about the tumor does not simply indicate targeted treatments, but rather has to be “made” actionable through complex collaborative work, often while a patient is very ill or near the end of life.

Identification of one or more actionable variants in the patient’s tumor DNA was encouraging news, but was often just the beginning of a lengthy journey through a dense bureaucracy of clinical trials, regulatory agencies, insurers, pharmaceutical companies, and ethics review boards. To facilitate access to experimental drugs, clinicians alternately referred patients to clinical trials, sought approval to use an investigational therapy outside of a clinical trial through “compassionate use” programs, created “n-of-one” trials with a patient as the sole participant in order to gain access to an investigational drug, or tried to persuade insurance companies to pay for “off-label” use of a drug approved by the U.S. Food and Drug
Administration (FDA) for the treatment of a different type of cancer. Following any one of these routes was arduous and not a path that all clinicians were equipped to undertake, as summarized by an oncologist:

I have done genetic studies on patients where I would get a defined mutation and I would get a very good hypothesis for a drug and then I try to get access for this patient to that drug. It is not just, “Oh, here is a clinical trial, go on it.” That is the simplest way. Often times I have to try to get compassionate use for the drug, that requires an FDA application, an IRB application … there is a lot of work that goes into it. It is more work than people want to do. It is more effort.

Despite their frustrations with the work involved in seeking a targeted treatment for a patient, most of the oncologists I spoke with appeared to throw themselves into the task with determination and persistence, and with a sense of moral obligation to their patients:

I just had a patient with kidney cancer, I was trying to get him this new drug that is actually FDA-approved for kidney cancer and the insurance company came back and said, “He does not have the subtype that was tested in the study, therefore we are not going to pay for it until you show me a Phase 3 study that” – I was like, “That is bullshit. You are never going to have a Phase 3 study in this rare type of kidney cancer.” They are just trying to pass the buck. I was ready to literally punch a wall with this. I usually do not get that upset but this freaking insurance company – I am like, “Look, this kid is dying of cancer … needs to get this drug.” Finally we got it through the company’s compassionate use program but it took a while.

As demonstrated in this account, clinicians worked to render a genetic mutation actionable through emotional labor, negotiation skills, knowledge of the clinical trials landscape. Considerable effort was also required from patients and caregivers, who often dedicated themselves to understanding “the whole clinical trial ecosystem,” as one patient phrased it. Clinicians and patients weighed the potential therapeutic benefits and side effects of experimental drugs and discussed whether the patient should commit time and resources to participate in a clinical trial, which may require long-distance travel. This collaborative labor was illustrated in an hour-long clinic session that I observed with Raoul, who had been undergoing cancer treatment for several years, and his oncologist, David. David and Raoul have a comfortable rapport that suggests a long and trusting relationship. David emailed Raoul a few days ago with a summary of Raoul’s genetic test results and today’s meeting delves more deeply into the results and their therapeutic implications. Looking at the lab report, David describes several “pathogenic” alterations found in Raoul’s tumor DNA and that may be actionable. There are a few drugs worth considering, he says. The first is being studied in a clinical trial that has two downsides: it requires biopsy tissue from participants and has been paused for the time being due to “technical difficulties.” Nonetheless, before today’s meeting David contacted the pharmaceutical company conducting the trial and requested permission to prescribe the drug for Raoul. He was turned
down. “They are not willing to give me compassionate use, just do not want to be bothered,” he says in frustration.

David then describes another clinical trial underway with a therapeutic agent that would target a second alteration in the tumor DNA. Unfortunately, he says, the study is not well designed and would require Raoul to travel across the country twice a month. They briefly discuss the trial and then decide against enrolling Raoul participation, mainly because of the faulty study design.

Raoul reminds David that he is reluctant to enroll in a “phase 1” clinical trial, in which the safety of a new treatment is tested, because of his concern about the potentially toxic effects of new drugs. They agree to set their sights on a third investigational drug. Raoul is not eligible to enroll in the clinical trial in which the drug is being studied because his disease is not advanced enough, but David has already made multiple phone calls to the pharmaceutical company sponsoring the trial in an attempt to secure a “single-patient exemption” that would enable Raoul to enroll in the trial. The sessions wraps up with David promising to call in a few days to let Raoul know if he was able to secure the exemption.

These efforts to render a variant actionable were taxing for both clinicians and patients, especially for patients who were suffering from the complex physical, social and emotional effects of their disease and treatment regimens. At the same time, however, the work was generative — reinforcing relations of mutual obligation and trust, enabling clinical research to move forward, and re-invigorating hopes for imagined individual and collective futures. Hope was never far from despair, but hope was also a practice that pushed against despair (Mattingly 2010).

When I interview Raoul a month later, he explains that the exemption request was denied but he remains enthusiastic about what he learned about the genetics of his disease. “To know more is to be able to grapple with it more,” he explains, conceiving of genetic information as both a tool that helps him to think about and live with his disease and as linked to a broader enterprise that promises an extended time horizon: “I am just trying to survive long enough that things catch up,” he says.

The effort to render a mutation actionable could also be generative beyond the patient’s life, not only through the contribution of one’s data to a larger research enterprise but also through the personal changes that family caregivers told us that they experienced. One day I spoke with Jennifer, whose husband William died of cancer a couple of years ago. She tells me that a mutation found in William’s tumor indicated that he could benefit from a therapy that had been approved for a different type of cancer but was being studied as a potential treatment for William’s type of cancer. They learned about a clinical trial that had recently concluded. The unfortunate results contained a glimmer of hope for William and Jennifer: “all of the patients died except for one who had the same mutation that my husband had … that was what we were pinning our hope on,” she said.
Their insurance company would not pay for the drug because there was not enough evidence of its efficacy, so Jennifer and William decided to purchase it themselves: “Okay, all right, let’s just buy it and do the fight later,” they reasoned. Their cost was US $10,000 per month during the two months that they spent contesting the insurance company’s decision. After four attempts to reverse the decision, they filed an appeal with the state that included a letter from William’s oncologist describing his encouraging response to the new treatment. They won the appeal and the insurance company was forced to pay for the treatment. The new drug was not a cure, she said, but it extended William’s life for a precious few months and the experience fighting for it had transformed her life. After William’s death she changed her career, becoming a writer and advocate for patients with William’s type of cancer. “I do feel like it was successful …,” she said, “… I think it [the drug] has the potential to be very successful for some people.”

Jennifer and William’s course of action was both a deeply personal effort to grapple with William’s disease and a contribution to the building of precision medicine through the addition of William’s genetic information to the medical center’s growing database. Jennifer’s agonizing fight to obtain the drug, similarly, was an act of caring for her husband that eventually led her to work on behalf of other patients. In this way, the work of keeping a loved one alive is bound up in efforts to achieve precision medicine’s potential. The question prompted by a story like that of William and Jennifer, however, is how participation in this future-oriented endeavor is distributed. A different sequence of events would undoubtedly have unfolded if Jennifer and William had not been able to pay $10,000 per month for the treatment, or if Jennifer and the oncologist had not been able to mobilize sufficient knowledge and cultural capital to overturn the insurance company’s decision.

Conclusion
In describing the shifting relationship between “medicine as an experimental system and medicine as an ethics of care,” Catherine Waldby (2012, 179) offers new ways of thinking about the labor that propels a contemporary economy focused on service and innovation. In an innovation-oriented bioeconomy, she says, “the entrepreneurial subject of health is one who enrolls their body’s capacities into a broader productive calculus, where the consumption of medical innovation is not clearly distinguishable from its production” (Waldby 2012, 182). The emerging enterprise of molecular oncology in the U.S. offers a compelling example of one such bioeconomy in which contribution and benefit, and present realities and future potential, are meshed and inextricably linked to financial markets and the creation of biovalue. This can be seen in the simultaneous use of patients’ genetic information for identifying and procuring targeted therapies and for the development and marketing of these therapies.
I have offered a close examination of this emerging bioeconomy at a U.S. academic medical center, focusing in particular on how clinicians, patients and caregivers collaboratively deployed knowledge, resources, biospecimens and future-looking narratives in an effort to arrive at precision medicine’s promise of personalized treatment. Their labors were both enabled and constrained by the structures of U.S. healthcare, including insurance coverage and reimbursement policies, the clinical trials industry, and the complex institutional landscape of health care delivery. Thus, what could be hoped for and accomplished, and who was able to participate, was inextricable from the broader social, political and economic forces shaping biomedical innovation and the delivery of health care.

How, then, to conceptualize potentiality as a defining idiom of precision medicine? On the one hand, a focus on technoscientific potential sustains hope in the possibility of life extension and prompts fervent activity and investment in support of this collectively imagined future; on the other hand, the potential of genomic medicine is allocated by way of the financial interests and inequities of a market-driven health system. If potentiality “makes moral claims on others to act” (Taussig, Hoeyer, and Helmreich 2013), we need a better understanding of who is participating in this field of action and what the consequences are for those who are not.

As molecular oncology initiatives proceed, I encourage closer attention to access and equity issues. Those guiding such initiatives should map who is able to contribute to and who benefits from the development and allocation of targeted cancer treatments. Equally important is understanding whether the data being collected ultimately serve to mitigate or exacerbate existing biases in genomic repositories resulting from the historical exclusion of racialized populations from genomics research (Popejoy and Fullerton 2016). In conclusion, I argue that efforts to sustain and propel the emerging enterprise of molecular oncology should be conceived as a moral bioeconomy – a social arrangement of “reciprocal responsibility” that requires constant attention to questions about who donates, who benefits, and who “falls out from the precision medicine pipeline…” (Lee 2020, 5). Without greater attention to how potential is allocated, the imagined future of precision medicine will remain promising while its on-the-ground initiatives (re)produce health inequities in the present.

Notes

1. “Precision medicine” is the term used most often in the U.S. to refer to the use of genomics to inform diagnostic, treatment and disease prevention practices, whereas “personalized medicine” is more common in Europe. See Juengst et al. (2016) and Erikainen and Chan (2019) for an analysis of the social, ethical, economic and political implications of the varied and shifting nomenclature in this emerging assemblage of practices and technologies.

2. In U.S. healthcare, the insurance industry’s coverage and reimbursement policies form a powerful mechanism by which new procedures and therapies become “standard of care” and patients’ needs and expectations are shaped (Kaufman 2015).
3. An oncologist at a public hospital that is affiliated with the academic medical center, and serves a high proportion of uninsured and publicly-insured patients, told me that her patients do not have access to the gene panel, presumably due to a lack of insurance coverage.

4. A tumor’s genetic profile can change over time, whereas genetic sequencing produces a representation of this complex, changing system at just a single point in time. As a consequence, clinicians and patients have to weigh the potential advantages of earlier testing (prudent use of limited biopsy tissue and reassurance for the patient) with its downsides (the possibility that results will become less accurate over time).

5. The private, for-profit laboratory’s practice of waiving the fee for tumor testing prompted consternation among our informants, some of whom were concerned that it would put academic, not-for-profit laboratories out of business. For uninsured and publicly-insured patients, however, the laboratory’s panel was the only point of access to tumor sequencing.

6. Biopsy tissue usually contains a mix of tumor and normal cells and tumor cells themselves can be genetically diverse, so an adequate supply of tissue is essential for accurate sequencing results.

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