Organizing precision oncology: Introduction to the special issue

Pascale Bourret, Patrick Castel, Henri Bergeron, Alberto Cambrosio

Organizing precision oncology: Introduction to the Special Issue

Pascale Bourret,[1] Patrick Castel,[2] Henri Bergeron,[2] and Alberto Cambrosio[3]
[1] Aix Marseille Univ, INSERM, IRD, SESSTIM, Marseille, France
[2] Centre de Sociologie des Organisations, Sciences Po, Paris, France
[3] Department of Social Studies of Medicine, McGill University, Montreal (QC), Canada

This is a post–peer-review, precopyedited version of an article published in New Genetics and Society. The definitive publisher-authenticated version [Pascale Bourret, Patrick Castel, Henri Bergeron & Alberto Cambrosio (2021) Organizing precision oncology: introduction to the special issue, New Genetics and Society, 40:1, 1-6, DOI: 10.1080/14636778.2021.1883501] is available online at URL : https://doi.org/10.1080/14636778.2021.1883501

This Special Issue (SI) on "Organizing precision oncology" features a number of articles initially presented at an International Workshop on "Organizational and epistemic innovation in precision cancer medicine" that took place in November 2018 in Paris. The Workshop was convened to mark the conclusion of a project supported by the French National Cancer Institute (INCa), entitled "Targets and trials: A sociological investigation of personalized cancer medicine in action (PERSONA)." The papers included in the SI have been revised and updated to reflect developments in the two years since the workshop was held. As hinted by the title of the Workshop, they investigate the implementation of precision oncology by focusing on the nexus between organizing and experimenting. The SI thus includes contributions that interface Science & Technology Studies (STS) and Organization Studies to analyze how clinicians and researchers deploy genomic platforms (Cambrosio et al. 2018) and the socio-technical and organizational arrangements that act as a condition of possibility for the performance of this new kind of clinical medicine

According to the 2020 Annual Report of the Personalized Medicine Coalition (PMC; http://www.personalizedmedicinecoalition.org)[1] -- an "international, multi-stakeholder, non-profit organization" for promoting the eponymous domain – the number of individualized medicines on the US market grew by 116% during the previous four years, and more than 75,000 genetic tests are available. In oncology, 61% of clinical trials now incorporate biomarkers compared to just 18% in 2000. In 2020, the FDA approved 27 precision oncology drugs, including 10 new molecular entities (NMEs) and 17 new indications of previously approved drugs, a 35% increase compared to the previous year (Staff Reporter 2021). These data point to a shift from the traditional focus on a tumor's tissue of origin to the genetic basis of the disease, as highlighted, for instance, by the "field's first tumor-agnostic drug approvals, in

[1] PMC members include clinical laboratory testing services, diagnostic companies, emerging and large biotech/pharmaceutical companies, industry/trade associations, IT/informatics companies, nutrition, health and wellness companies, patient advocacy groups, personalized medicine service providers, research, education, and clinical care institutions, research tool companies, strategic partners, and venture capital.

which a therapy is indicated based on the presence of a specific cancer biomarker regardless of a tumor's location in the body" (Ashford 2012). On the other side of the Atlantic, the November 2020 edition of the French Oncology Meetings (RCFr; https://rcfr.fr/), was devoted to a discussion of how the emergence of precision medicine is reconfiguring multiple dimensions of oncology practices, namely prevention and screening, therapy, technologies, organizational, societal, and health economics aspects.

We could multiply the examples, but this is hardly necessary. Even taking into account the usual dose of hype that accompanies the emergence and introduction of new approaches and technologies, it seems indisputable that a profound reassembling of practices is underway in the field of oncology. Reassembling, rather than "disruption", insofar as far from being entirely reborn from its metaphorical ashes, the performance of contemporary oncology is predicated upon the re-alignment of old and new entities and practices. As argued by Rabinow (2000, 44) and reiterated by Rheinberger (2009, 7) "from time to time, new forms emerge that have something significant about them, something that catalyzes previously present actors, things, institutions into a new mode of existence, a new assemblage, an assemblage that made things work in a different manner."

And yet, one can easily find examples of scholars (often philosophers and bioethicists, with the occasional oncologist[2]) who condemn the use of terms such as personalized and precision medicine as empty rhetoric, tainted by those terms' alleged promissory nature. According to some of these critics, physicians have been personalizing care and analyzing precise disease causes for centuries, evidence continues to be derived from and applied to groups rather than individuals, imprecision still characterizes medical practices, and, last but not least, promises of miracle cures remain largely hype (e.g., Tabery 2020). Some of these arguments might be worthy of consideration, especially when reflexively deployed by practitioners, in which case, however, we should examine them "as substantive constituents of a dispute, rather than as sources of validation for a general line of sceptical argument" (see Lynch 1998, 856 on the topic/resource distinction). But, like Eyal et al. (2019), we disagree with the "cynics'" objections and favor a very different approach. Rather than stigmatizing the inappropriate use of terms and the alleged interests that underlie their use, we consider that there is no such thing as "mere rhetoric," and opt for a detailed empirical investigation of the motley of precision oncology's initiatives and activities that are labeled as such. We call for an examination of the organizational, epistemic, socio-material, and discursive dimensions of emerging routines (Feldman *et al.* 2021), including, of course, those implicating the patients who, confronted with these opportunities, make their own body available by accepting to undergo genomic testing and participate in clinical trials of experimental and off-label drugs. In other words, rather than asking whether there is such a thing as precision oncology, we study its actual performance. As argued by Ian Hacking (1983, 23) in an admittedly quite different context, "So far as I'm concerned, if you can spray them [electrons], then they are real".

[2] Vinay Prasad is one of the fiercest critics of Precision Oncology from within oncology's ranks; see, e.g., Prasad (2016), and Subbiah and Kurzrock (2017) for a rebuttal.

The molecular approach and related high-throughput technologies at the core of precision oncology associate clinical oncologists and pathologists with molecular biologists and bioinformatics specialists, modifying the equilibrium between the traditional components of oncology. In other words, precision oncology relies on a complex landscape of interrelated resources and platforms that, if properly coordinated, engender huge amounts of heterogeneous data in need of consistent, appropriate interpretation. As a result, oncology has become to a significant extent a data-centric domain (Leonelli 2016), generating more information than can be readily interpreted by individual practitioners. While genomic platforms contribute to the (re)definition of clinical activities, the mobilization of their findings takes place within settings already shaped by pre-existing laboratory and clinical routines and models, both organizational and epistemic. As mentioned, innovations must contend with their necessary articulation with established clinical practices, a process that is a source of constant friction and that has transformed the translational pathway from genomics to the clinic into a rocky road. Clinical judgement has long been deployed in a dense web of laboratory measurements and techno-scientific mediations (Rheinberger 2011). By exhibiting many traits of data-centric activities, genomic medicine adds layers to these processes. The clinical interpretation of genomic sequences is accomplished via a world of mediators, including databases and data processing algorithms. Accordingly, clinical teams are increasingly required to interact with bioinformaticians and computational biologists. Genomic platforms have also led to the emergence of an entire sector of commercial providers for the production and interpretation of genomic results. Available academic and commercial decision support technologies act as *de facto* regulatory tools and devices, and their prodution has generated, in turn, calls for meta-regulation. Understanding precision medicine thus requires continued attention to the resources, opportunities, and constraints created by academic, commercial, and increasingly hybrid practices and initiatives.

Individual contributions to the SI address the issue of how local contexts constrain and frame the design and performance of genomic practices, and how, in turn, these practices reconfigure local contexts. This involves investigating changes concerning clinical routines, the context and modalities of clinical expertise and decision-making, the growing reliance on databases and algorithms, the organization and activities of biology and pathology laboratories, and the redefinition of collaborative patterns and the division of labor between health care professionals, patients, researchers, and pharmaceutical companies.

Steve Sturdy's paper examines the historical roots of contemporary precision oncology, focusing on the early emergence of bioclinical collectives and hybrid practices, initially confined to the hereditary cancer domain. For each type of familial cancer, different configurations of actors, organizations, and resources were put in place to meet the objective of discriminating ever more precisely between cancers, patients, and mutations. This kind of precision research initiated a process of differentiation reaching out to present-day precision oncology. Moving to the contemporary period, the paper by Chiapperino *et al.* examines an example of precision oncology's architecture, using the notion of epistemic dwellings to explore how architecture does not merely reflect developments in the biomedical field, but actively contributes to them, partaking in the reconfiguration of practices and their coordination across professional lines.

The paper by Castel *et al.* focuses on this latter aspect but from a different perspective, exploring how the promotion of precision oncology initiatives by the French National Cancer Institute has led to organizational conundrums that can be accounted for by examining the constraints of collective action and related coordination activities, rather than jurisdictional struggles or the presence of different "thought styles".

Tempini's paper centers on the creation of a new information technology infrastructure that acts as a condition of possibility for the performance of precision oncology practices, namely the establishment of data- and knowledgebases. Resorting to James March's (1991) classic distinction between exploration and exploitation, the paper investigates the dynamics of innovation and change by focusing on a new kind of scientific activity, namely data-curation research. Relatedly, Cambrosio *et al.* investigate the new decision-making settings known as Molecular Tumor Boards (MTBs) within which the kind of curated knowledgebases analyzed by Tempini are deployed. Beyond the analysis of the internal dynamics of MTBs, the paper examines how the switch from a diagnostic to a theranostic approach that is embedded in MTB deliberation has consequences for the redefinition of the looping relation between diagnosis and therapy, but also for genomic medicine's understanding of the very notion of diseases as natural entities. Finally, Kerr *et al.* examine how patients reposition themselves vis-à-vis precision oncology. Escaping traditional interpretations of patient activism, their paper analyzes how patients, their caregivers and advocates build networks to gather support, comparing UK cancer activism to how similar work is performed in other countries. The paper thus highlights the diversity of advocacy work and capacity for critique, arguing that in addition to knowledge work, emotional work that mobilizes a plethora of emotions beyond hope is involved in advocacy.

Although they differ in their subject matter, theoretical questions, and methods, the articles presented here share a common interest in investigating how shifts in practices, roles, or jurisdictions are predicated upon intense organizational work and how, in turn, organizational innovations rely on technoscientific experimenting: whether the issue is to design the architecture of new premises that organize the workspace in a novel way in order to align practices, therapeutic trials, and epistemic approaches; to elaborate new organizational arrangements to modify the perimeters of professional jurisdictions and transform relationships and the division of labor; to build new networks in order to modify the forms of commitment of patients and patient advocates; or to build the IT and decision support infrastructures necessary for the exploitation of vast databases in order to deploy a new type of scientific activity, organizational work seems to be one of the essential mediations in the transformation of practices and reasoning engendered by precision medicine. A detailed analysis of the emergent dynamics of these organizational arrangements is a key component of any investigation of the mechanisms promoting the reconfiguration and reassembling of biomedical research and practices in the post-genomic era.

For obvious reasons, this SI does not pretend to cover all aspects of the complex set of initiatives that fall under the umbrella of precision oncology. All papers are grounded in empirical investigations of North American and European settings: any discussion of what is

presently known as “the Global South” and its contributions to cancer genomics is conspicuously absent. Except for a few in-passing remarks, the pharmaceutical, biotechnology, and medical technology industries are also not the focus of this collection of papers despite the central role they play in the development of precision oncology. This is partly due to the difficulties in conducting fieldwork and collecting commercially sensitive information at the oncology research front (see Timmermann 2019 for a recent exception, albeit one directly sponsored by the pharma company featured in the book). Readers will certainly point to other omissions, which can at least in part be accounted for by our bias of favoring texts with a robust empirical basis rather than speculations about possible developments. We hope, however, that despite its limitations this collection of articles will contribute to the collective, ongoing work of analyzing the organizing and experimenting processes at the core of precision oncology as a pioneering domain of “omic” medicine.

References

Ashford, Molika. 2020. “PMC Report Outlines Strong Growth, Future Challenges for Personalized Medicine Industry.” *Precision Oncology News.* https://www.precisiononcologynews.com/clinical-sequencing/pmc-report-outlines-strong-growth-future-challenges-personalized-medicine#.X9Ymz157nGI.

Cambrosio, Alberto, Etienne Vignola-Gagné, Nicole Nelson, Peter Keating, Pascale Bourret.2018. “Genomic Platforms and Clinical Research.” In *Routledge Handbook of Genomics, Health & Society,* edited by Sahra Gibbon, Barbara Prainsack, Stephen Hilgartner, Janelle Lamoreaux, 142-150. London: Routledge.

Eyal, Gil, Maya Sabatello, Kathryn Tabb, Rachel Adams, Matthew Jones, Frank R Lichtenberg, Alondra Nelson, et al. 2019. “The Physician-Patient Relationship in the Age of Precision Medicine.” *Genetics in Medicine* 21 (4): 813-815.

Feldman, Martha, Brian T. Pentland, Luciana D’Adderio, Katharina Dittrich, Claus Rerup, David Seidl. 2021. “What Is Routine Dynamics?” In *Cambridge Handbook of Routine* Dynamics, edited by Martha Feldman, Brian T. Pentland, Luciana D’Adderio, Katharina Dittrich, Claus Rerup,David Seidl. Cambridge: Cambridge University Press (in press).

Hacking, Ian. 1983. *Representing and Intervening*, Cambridge: Cambridge University Press.

Leonelli, Sabina. 2016 *Data-Centric Biology: A Philosophical Study*. Chicago: University of Chicago Press.

Lynch, Michael. 1998. “The Discursive Production of Uncertainty. The OJ Simpson ‘Dream Team’ and the Sociology of Knowledge Machine.” *Social Studies of Science* 28: 829–868.

March, James G. 1991. “Exploration and Exploitation in Organizational Learning.” *Organization Science* 2: 71 87.

Prasad, Vinay. 2016. “The Precision-Oncology Illusion”. *Nature* 537: S63.

Rabinow, Paul. 2000. “Epochs, Presents, Events.” In *Living and Working with the New Medical Technologies*, edited by Margaret Lock, Allan Young, Alberto Cambrosio, 31–46. Cambridge: Cambridge University Press.

Rheinberger, Hans-Jörg. 2009. “Recent Science and Its Exploration: The Case of Molecular Biology.” *Studies in History and Philosophy of Biological and Biomedical Sciences* 40: 6-12.

Rheinberger, Hans-Jörg. 2011. “Infra-experimentality: From Traces to Data, From Data to Patterning Facts.” *History of Science*, 49: 337-48.

Staff Reporter. 2021. “Precision Oncology in 2020: Pandemic Lessons, Biomarker Controversies, Community Access Gaps.” *Precision Oncology News* (Jan. 5). https://www.precisiononcologynews.com/business-news/precision-oncology-2020-pandemic-lessons-biomarker-controversies-community-access-gaps#.X_WduOAo_GI

Subbiah, Vivek, and Razelle Kurzrock. 2017. “Debunking the Delusion that Precision Oncology Is an Illusion.” *The Oncologist* 22: 881–882.

Tabery, James. 2020. “’Personalized Medicine’” Wasn’t Personal; ‘Precision Medicine’ Isn’t Precise.” https://www.philinbiomed.org/event/james-tabery/

Timmermann, Carsten. 2019. *Moonshots at Cancer. The Roche Story.* Basel, Editiones Roche.