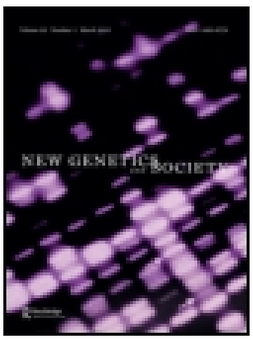

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Organizing the precision clinic: arranging expertise, knowledge and technologies in cancer precision medicine clinical trials

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The aim of this article, which draws on qualitative research focussed on working practices around a genomic-informed clinical trial, is to contribute to the ongoing debate on how care professionals and biomedical investigators mobilize collective expertise *in* and *across* organizational settings to shape so-called precise knowledge in cancer medicine. In so doing, the paper discusses three interrelated issues concerning the day-to-day practices of those doing what they are supposed to do to produce knowledge capable of enacting a precision oncology regimen: (i) *situatedness and reshuffling of the professional jurisdiction* (work always takes place in a texture of practices influencing how the work is understood and carried out); (ii) *organizing technologies* (mobilization of different kinds of medical technologies to produce knowledge when carrying out work practices as a vehicle for epistemic negotiation); and (iii) *articulation work* (the centrality of cooperative work to enact trial work).

Keywords: precision medicine; genomics; oncology; knowing in practice; biomedical practices

1. Introduction

In recent decades, greater recognition of the fact that each individual may require a specific form of therapy for their tumor has brought the work of life science research to quick fruition. This is fueling a collective production of evidence where biomedical practices are combining in novel ways biology and clinical domains as well as biological entities (e.g. nucleotide bases and their variations, organ tissues, etc.), clinical instruments and genomic-based technologies.

Notwithstanding the circulation of promissory claims about the alleged dominance of genomic sciences and biological breakthroughs in the clinical setting, what it is at stake in redefining contemporary biomedicine is a deep interlacement of technologies operating at the molecular level (primarily related to functional

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properties of coding sequences of nucleotide) with molar equipment (operating at the level of organs, tissues, and so on; see Rose 2007) to enhance knowledge translation for healthcare improvements. This kind of *hybridicity* (Latour 1999) between biology and medicine is at the core of the current precision medicine clinic, where information about variabilities in a person's genes, lifestyle and environment is collectively channeled to improve the accuracy in defining treatment and prevention strategies for a particular disease.

Unsurprisingly, oncology is particularly committed to boosting precision medicine with the aim of designing therapeutic options for cancer patients by mixing traditional molar drug administration evaluation factors (e.g. age, body mass index and sex) and clinical variables with the patient's genetic profile and tumor molecular alterations (Aronson and Rehm 2015). Personalized cancer treatments underpin the enactment of heterogeneous expertise rooted in different biomedical domains (e.g. clinical oncology, molecular biology, data science, experimental pharmacology and nursing) so as to combine and interpret significant bodies of clinical and genomic data for informing tailored therapeutic decisions. Accordingly, novel organizational arrangements and collective expertise are emerging in the field of oncology with the aim of assessing the clinical relevance of genomic signatures, such as predictive biomarkers. This is driving the readjustment of methodologies rooted in cytotoxic chemotherapy trials to molecular diagnostics to predict if, and to what extent, individual patients respond to a particular chemotherapy protocol.

Thus, cancer precision medicine is soliciting the uptake of a complex process of aligning existing clinical routines, conventions and standardized treatment approaches with new genomic-based technologies and knowledge as they make their way to the clinic (Cambrosio *et al.* 2018). In this respect, it is crucial to understand what such technological entanglements between the *molar* and the *molecular* imply for cancer healthcare and research organizations, their norms and forms of structuring, their capabilities to act and interact, and their possibilities for innovation and learning. In other words, *what is it that clinicians and biomedical investigators actually do when they are doing their job on implementing the precision medicine clinic in practice?*

Despite the increasing reliance of current clinical oncology on molecularly targeted agents and prognostic and predictive biomarkers, we know surprisingly little about what the situated work of care practitioners (e.g. clinical oncologists and nurses) and biomedical researchers (e.g. molecular biologists and experimental pharmacologists) entails in producing (bio)knowledge[1] capable of informing cancer precision medicine. In this respect, *what counts as "precise knowledge" when practising cancer precision medicine?*

The above questions encourage an examination of the epistemic stance of precision knowledge by investigating how different medical technologies and expertise (both at the clinical and laboratory levels) are mutually entangled in the organization of work routines for shaping tailored cancer protocols. To grasp such an issue, it is fruitful to rethink the standard analytical approach for exploring

the modalities of (bio)knowledge production at large, traditionally addressed within social sciences by postulating an epistemological bifurcation of the *logic of care* – unfolded for the sake of the patient – and the *logic of discovery* – unfolded for the sake of science (Blume 2013). This dichotomy elicits a sort of incommensurability between the style of reasoning behind care expertise and that enacted by biomedical researchers, thus hampering an understanding of the translation in practice of current procedures and trials for precision oncology. Therefore, the issue of how clinical staff and biomedical investigators work and mobilize expertise *in* and *across* cancer organizational settings to pursue experimental protocols and fabricate clinically actionable knowledge is neglected. Theoretically speaking, the reason for this lack of interest in exploring the entanglement of heterogeneous biomedical expertise and technologies can be traced back, on one hand, to the conception according to which the (structural) conditions of (bio)knowledge production are generated and enacted in the course of social action and, on the other hand, to a vision that frames social structures as the determinant of conditions for (bio)knowledge production.

Given this state of affairs, this paper focusses on the day-to-day practices and experiences of researchers and clinical staff and their learning biographies of doing what they are supposed to do to produce actionable precision knowledge within genomic-informed oncology clinical trials. Specifically, the attention revolves around practices – both discursive and material – emerging in the situated settings of interaction aimed at predicting relationships between clinical/genomic information and cancer drug therapies. This paper avoids discussing socio-epistemic relations between the clinic and the laboratory in terms of subordination. Instead, it considers knowledge in the context of cancer precision medicine as an *act of knowing in practice* (Gherardi 2019; Orlikowski 2002) which mediates relations between technologies, materials and heterogeneous biomedical expertise at work. Under this lens, relationships between the clinic and laboratory-based practitioners cannot predetermine the meaning and content of the concerned precise knowledge, since the content of knowledge itself is an emerging outcome and a constitutive element of such relationships. At the same time, organizational arrangements are performed and transformed at the interface between clinical and laboratory settings. Accordingly, the focus on knowing in practice enables the disclosure of expertise and heterogeneous arrangements in producing so-called precision knowledge as a practical performance rather than as a linear transfer of knowledge or as processes that merely extract data from living bodies.

2. Methodology

This paper is rooted in a qualitative, field-based study conducted within a major biomedical institute in northern Italy which specializes in cancer care and research. It is a cancer hospital acting within the translational medicine framework (see Crabu 2018), thus promoting fundamental and clinical research activities along

with caring for cancer patients. Fieldwork at this site primarily focussed on the management of genomic-informed clinical trials, which rely on molecular diagnostics for predicting whether patients will benefit from concerned chemotherapy protocols and, if not, sparing them ineffective treatment.

Empirical research was characterized by methodological triangulation using three main techniques: interviews, in situ observations and document analysis (predominantly protocols, laboratory diaries and internal reports) to explore the various actors, identities, cultural meanings and research-related technologies engaged in conducting a Phase 1 genomic-informed clinical trial for identifying tailored therapeutic options for colorectal cancer patients according to their molecular pathways. In this respect, the trial identifies a valuable empirical entry point to explore how the enactment of precision knowledge from living bodies intertwines with everyday working practices, implying the acquisition of novel professional roles and of expertise in knowing how to do things in a certain way for locating a genomic-informed trial protocol at the interface between the care and laboratory sites.

Observations were conducted for six months. During this period, daily activities within the research laboratories and hospital wards were monitored. Handwritten field notes were taken during observation days and 14 semi-structured interviews were conducted with laboratory researchers, molecular biologists, pharmacologists, chemists, data managers, clinicians, research nurses and scientific officers of the biomedical laboratories. Drawing on in situ observation and actors' narratives about their everyday practices, the findings focus on the socio-technical microdynamics of work to study how laboratory staff and clinicians negotiate practical problems in defining precision knowledge in the context of genomic-informed trials. In so doing, the paper discusses three interrelated issues that, when considered together, outline precision medicine as a practice: (i) situatedness and reshuffling of the professional jurisdiction (work always takes place in a texture of practices influencing how it is understood and carried out, taking into account professional boundaries); (ii) organizing technologies (mobilization of different kinds of medical technologies to produce (bio)knowledge when carrying out work practices as a vehicle for epistemic negotiation of the content of precise knowledge); and (iii) articulation work (the centrality of a specific kind of interprofessional cooperative work to to enact trial work). Given the paper's focus, the presentation of findings follows a narrative strategy proposed by scholars such as Jackson (1990), Rapp (2011) and, more recently, Lewis, Hughes, and Atkinson (2014), according to which empirical materials are not merely mobilized as free-standing pieces of data but, rather, as an empirical trigger to both explore and theoretically capture biomedical and organizing practices of the clinic of precision. Accordingly, the pieces of data are combined into enlightening ethnographic episodes with the purpose of tracing and following precision medicine phenomena across the different sites of (bio)knowledge production. Each episode is framed as an instrumental case study (see Stake 1994) designed to provide insight into

specific relevant issues and instances related to the way actionable precision knowledge can be enabled.

3. Findings

3.1. *Episode 1: situating expertise within the bio-clinical texture*

In the context of cancer precision medicine, biomedical work involves combining genomic-based knowledge (elaborated through laboratory activities) with existing clinical procedures, technologies and records to render signaling molecules actionable to design drugs and therapeutic strategies for specific patients. The rationale behind tailoring treatment to suit the characteristics of each patient (and his/her disease) is grounded in developing knowledge about clinical and molecular pathways, which can be further examined via the adopted drug:

> We are evaluating how certain polymorphisms of "UGT"[2] allow treatment with higher doses of the drug, because they show a lower toxicity and a better clinical response. […] Patients are treated with different doses depending on their body surface and genotype. The amount of the drug should be assessed by a physician. (Pharmacologist involved in a Phase 1 genomic-informed clinical trial aimed at personalizing treatment for patients presenting with colorectal cancer)

Within precision medicine clinical trials, the patient is framed as a biological setting where practices aimed at establishing a specific gene polymorphism as a "druggable" biomarker are located. Thus, the issue at stake is not so much information and technology transfer (e.g. diagnostic tests, genetic screening and medical records) from one site (i.e. the laboratory) to another (i.e. the clinic) and vice versa. Rather, it is a matter of enacting an interactive hybrid forum engaging clinical staff and biomedical researchers in studying and establishing the clinical relevance of biomarkers for predicting chemotherapy outcomes in individual patients. Such studies aimed at readjusting clinical trial methodologies developed in the context of cytotoxic chemotherapy to molecular diagnostics raise issues beyond mere technical concerns, as novel protocols solicit organizational learning processes and the shaping of ad-hoc expertise (Crabu 2014). Indeed, genomic-based information must be juxtaposed with clinical records of the course of the disease in relation to the administered chemotherapy. The following account exemplifies this point – namely, that the production of precise knowledge is multi-sited and located within spheres of interdisciplinary work and entangled with an emergent bio-clinical texture:

> Well, only in very rare cases, I might continue to prescribe a CT scan every two months for patients who are no longer eligible for clinical trials […] It is quite another matter when you work within an experimental protocol: the rules of the game are quite different, and it involves different colleagues as well. In fact, reassessments with CT scans will be scheduled every month-and-a-half because they are important for the study; I mean, for instance, for the experimental staff studying

> drug metabolism, and not because you want to be closer to the patient … (Oncologist involved in a Phase 1 genomic-informed clinical trial aimed at personalizing treatment for patients presenting with colorectal cancer)

This excerpt draws attention to the alignment of heterogeneous expertise at work: laboratory-based researchers and clinicians – with their shared priorities, decision support systems, conventions and regulatory ethos – circumscribe a bio-clinical texture in which the trial, bridging biology and clinical medicine, can be imagined and performed. This requires the coordination of different genealogies of technical apparatus, such as molecular diagnostics with imaging technologies. This aspect underscores the fact that the unfolding of hybrid clinical-experimental actions to produce actionable precise knowledge and the capacity of such clinical-experimental actions to reshuffle organizational and epistemological boundaries between the clinic and the laboratory are neither intrinsic to specific genomic developments nor simply depend on the physician's competence framework and professional jurisdiction. In this regard, scholars have learned much by approaching (post-)genomic technologies as a specific organizational technique (i.e. in redefending biomedical organizing rules and conventions) for producing novel therapeutic outcomes. However, such analytical primacy over genomics may obscure ways of seeing how organizational practices and relations for collectively elaborating cancer precision knowledge always entail some sort of entanglement of molar and molecular techniques. Accordingly, it is crucial to not consider this entanglement as an occasional or separate organizational phenomenon, so as not lose the possibility of capturing how this is a constitutive part of all organizing at all times and in all settings and circumstances of a cancer precision clinic. Indeed, genomic-informed clinical trials enact socio-technical processes on the basis of patients' genomic, clinical features and specific disease trajectories. This occurs according to the peculair experimental arrangements within the clinical trial as a crucial dimension of the evidence constructed and discussed by the clinical and laboratory staff both when managing individuals to produce (bio)knowledge and when making diagnostic and therapeutic decisions. In so doing, clinical routines are realigned with specific standards (not entirely ascribable to either the clinic or the laboratory) for assessing the safety and efficacy of specific novel therapies:

> I receive calls from the day hospital, and the ward oncologist says, "Listen, this patient has neutrophils at 2.200. Do I give him the therapy [i.e. drug infusion] or not?" I mean, then you tell him that at 2.200 it might be better to postpone the infusion to the next day because the patient might improve, and we may also have neutrophil values at a more acceptable level … and well, I also seek the opinion of colleagues in the experimental unit … and then we schedule a blood count for the next day, to reconsider what to do. […] Okay, of course, this happens because I have the experience and knowledge developed from managing Case Report Forms. […] You have to, anyhow, read blood test results … the doctor does not write "anaemia grade 1"; "neutrophils grade 3" in the clinical record. Indeed, I can read the diagnostics and tell you what the toxicity level is, and I also discuss this with those who do

> pharmacokinetics. In short, I can tell you whether the anaemia is caused by the drug you are taking or if it is related to the disease or another event. So, I can also give you a correlation. I can take a report from a radiologist and compare it with other information to see the response to infusions or if the disease is progressing. (Data Manager involved in a Phase 1 genomic-informed clinical trial aimed at personalizing treatment for patients presenting with colorectal cancer)

This quotation invites engagement with the complexity and equivocality that can be empirically observed in relations between different kinds of clinical and biological knowledge. Here, the data manager role encompasses multiple kinds of expertise and it is not centered around a homogeneous disciplinary core. Rather, the data manager performs a dual role situated at the intersection of clinical, biology and data management domains, thus shaping an epistemic commitment to the lab and the clinic. Indeed, the data manger, drawing on her clinical and data management expertise to support the fluid integration of different trial-work phases, clarifies that her daily work does not entail well bounded disciplinary expertise. Therefore, it is possible to appreciate precision knowledge as an effect of an array of relations grounded in both molar and molecular techniques that are not only reciprocally interdependent but also symmetrically relevant. By combining an in-depth understanding of research issues with a clinical appreciation of the challenges of implementing the protocol, the data manager can tailor the intervention to problems identified. The overlapping responsibilities in the data manager's work act as a knowledge-brokering mechanism to coordinate different types of data with their own epistemic structures or to solve contingent problems. In this way, the data manager is an intermediary who not only sorts information but participates in shaping its meaning. In this sense, knowledge brokering has the potential to interlace diverse forms of professional expertise transcending established specialist domains. Thus, such professional expertise can be more readily performed due to the closer, overlapping relations between the professional communities involved in the trial. What determines the appropriateness of procedures in a trial is not the protocol per se but the interplay between the clinical trial's specific organizing sites and the unfolding role enactment and situated work practices. In this regard, we can notice the emergence of a collective expertise that exceeds the discrete cognitive and professional perimeters of the laboratory and the clinic. Indeed, the decision to postpone the infusion was based on diverse bio-clinical considerations. From an analytical perspective, this allows for a different understanding of the clinical decision-making process, which is not based on the clinician's primacy and supposedly proceduralized knowledge and ability but, rather, on the capacity of the concerned professionals to collectively negotiate and shape seamless intersections in the bio-clinical network (inherently interdisciplinary) when continuously facing contingent challenges and reshaping their own activities. In this sense, decision-making over patient management is no longer related only to medical oncology, and it is not confined by disciplinary boundaries; instead, it traverses various domains, since it is distributed in an interdisciplinary network supporting the

production of precise actionable knowledge through the involvement of the patient's living body.

3.2. *Episode 2: mobilizing technologies for precision knowledge*

The previous episode framed precision medicine as not simply a novel context-free concept embedded in a (post-)genomic landscape that pervades oncology from without. Rather, it qualifies a texture of practices that influences and reshuffles professional boundaries and medical jurisdiction over the patient's body. The second episode takes the analysis a step further by showing that cancer precision medicine defines a socio-technical environment, which concerns, on one hand, technologies used in the process of knowledge production by means of a trial and, on the other hand, the (expected) outcomes of this process. This means that the distinctive feature of current precision medicine does not rely on post-genomic sciences themselves but on their epistemic bridges with clinical routines for producing actionable knowledge. Accordingly, it is crucial to explore technological solutions-in-use (Suchman *et al.* 1999) as devices located in the bio-clinical texture and with which laboratory and clinical professions cooperate to produce (bio)knowledge as well as to unfold diagnostic and experimental decision-making.

> I'm "shadowing" a PhD student within a small laboratory where machines to conduct high-performance liquid chromatography (HPLC)[3] are located. Pina [a senior experimental pharmacologist] and her assistant introduce the PhD student to the "experimental journey" to be conducted today, i.e. the analysis of plasma samples of two patients enrolled within the a genomic-informed clinical trial.
>
> Assistant: In this study, we have to understand the interaction between the FOLFIRI regimen and Bevacizumab in relation to the patient's genotype, or better to the mutations in the UGT1A1 gene. In fact, we collect samples as soon as irinotecan is administered, that is, without bevacizumab; and then we collect samples also after the administration of bevacizumab one hour after its infusion. By the way, the overall analysis will be done after 'assaying' [i.e. analysing the samples with the HPLC technique] all the patients, so that the data may have some statistical relevance; and also the clinical observations, or the diagnostic imaging can be referred to clear quantitative dimensions […]. (Ethnographic field notes on plasma sample processing within a Phase 1 genomic-driven clinical trial aimed at personalizing treatment for patients presenting with colorectal cancer)

This excerpt highlights that while biomedical technology-in-use may be viewed in terms of an infrastructural condition required to produce (bio)knowledge in the context of cancer precision medicine, such a condition cannot be appreciated without understanding its sociomaterial dimension. In other words, it is crucial to understand how technologies are enacted within the heterogeneous assembly of clinical and experimental expertise (i.e. experimental pharmacologists and

clinicians in charge of producing clinical observations), embedded standards, conventions and genres of information that give it meaning: a bio-clinical texture of practices for shaping relations with biological substances to be rendered meaningful by means of technical mediation. Indeed, the experimental pharmacologist and her assistant frame the HPLC as an information-generating agent to study the metabolism of drugs. This implies unfolding an ensemble of operations to align the patient's biology (or better, some specific clinical and molecular pathways correlated with the concerned disease) with the experimental protocol and its rules. In formal terms, one could argue that what is at stake here is merely the description of protocol rules. However, if we consider what it takes to translate the protocol into practice, it is possible to notice that the rules and bio-clinical specificities of the situations at hand (i.e. the validation of a method to produce information about the metabolism of drugs to be combined with qualitative clinical observation) are not two distinct domains. Indeed, bio-clinical specificities and rules work together in creating the sociomaterial context in which the construction of knowledge within a precise medicine regimen occurs. Here, the plasma sample processed by means of the HPLC technique should be considered an "epistemic thing" (Rheinberger 1997), a driver to shape knowledge enacted by arranging experimental conditions, institutionalized practices and shared skills. The object of investigation (the interaction between clinical circumstances, a gene mutation and a specific chemotherapy regimen) is, thus, articulated within heterogeneous epistemic and material conditions, such as machines, embedded theories and biological substances entangled in it. The dedicated machine adopted by the experimental pharmacologists is configured as a device to guide experimental decision-making and to produce clinically actionable knowledge, since the (qualitative) clinical modes of knowing (e.g. diagnostic imaging) must be epistemologically strengthened due to the conventions of quantitative objectivity in the laboratory field. At the same time, clinical observations offer laboratory staff situational awareness of the patient's disease and infuse relevant contextual meaning with laboratory-based evidence (e.g. quantitative signals on drug metabolism). Given the stratification of diverse technologies (i.e. some rooted in cytotoxic oncology, others in genomic oncology), many contextual features are explicitly mobilized for supporting translation activities behind the protocol. As the next ethnographic episode will further clarify, this involves a negotiation between the clinical and laboratory staff, who have their own conventions regarding how the safety and efficacy of potential genomic-informed therapies should be assessed. In this light, practising tailored oncology protocols constitutes a form of collective organizing and socio-technical change of existing biomedical practices, where professional roles can be taken up, challenged and renegotiated. Thus, performing precision medicine in practice implies conducting distributed, collaborative investigations at the nexus of the laboratory and the clinic, thereby enabling a co-production of epistemic things and related knowledge in a hybrid space – that is, a bio-clinical texture. This identify intersections of heterogeneous assemblages in which diverse professionals,

organizations active in the global healthcare sector (e.g. hospitals, biotech companies producing biotechnologies and laboratory machines) and other agents (e.g. bio-clinical entities and scientific instruments) cooperate in redefining the clinical and biological existence of cancer patients mobilized within cancer precision medicine clinical trials.

3.3 *Episode 3: articulation work and organizational arrangement*

The second episode clarified how the process of managing biological substances can be conceptualized as an ensemble of bio-clinical materially mediated practices, which intersect the laboratory and the clinic, aimed at configuring epistemic things within a precision medicine regimen. These practices are performed by various professional communities and sub-communities rather than by individuals, thus indicating that agents who generate precision knowledge should be framed as collective expertise emerging by materially mediated interdependencies across bio-clinical practices. As such, precision is both a claimed social and technical attribute, and its meaning and boundaries are never self-evident but are, instead, subjected to collective inter-professional negotiations:

> I'm in the premises of the department of clinical and experimental pharmacology. […] Pina's cell phone rings. She listens, without speaking. As the phone call closes, Pina explains:
>
> Pina: It was Lorenza [a research nurse]. She called me from the ward. We have to get there right now, because the infusion is already over. Lorenza has also already checked the infusion pump. It seems that it has administered 265 cc of the drug instead of 330 cc.
>
> Assistant: What? How did she see it?
>
> Pina: Well, you can notice it by reading the infusion pump monitor. Before the infusion, she [the research nurse] reset the pump and, then, at the end of the infusion, she verified the administered quantity of the drug. I guess they [the hospital pharmacy staff] were wrong in preparing the bag with the drug. Frankly speaking, I hope that Lorenza has already taken the blood sample at the end of the infusion. I need it to determine the Cmax.[4]
>
> We walk quickly towards the ward.
>
> Lorenza: I've already taken the blood sample. […].
>
> Pina: Well done. But at what time did you collect it, exactly? Since, I have to reschedule the next blood samplings accordingly.
>
> Lorenza: I did it four minutes ago. My watch showed 10:57.
>
> Pina: Okay. By the way, I should immediately check with the patient. Let's synchronize our clocks […]. Otherwise I miss the Cmax.

> […] Meanwhile, Pina comments in a low voice, "I'm quite confident … in case of problems I can ask the patient at what time the sample was taken. He is never wrong."
>
> (Ethnographic field notes on blood sampling within a Phase 1 genomic-driven clinical trial aimed at personalizing treatment for patients presenting with colorectal cancer)

This excerpt underscores a clear need to translate a complex protocol into detailed practical actions within the hospital ward to capture the biological material and information required to conduct laboratory investigations (i.e. the Cmax). Here, there are forms of work and socio-technical ordering produced by the distributed and mutually constituting agencies of professionals and different technical devices. Technologies for administering the drugs become tools for researching biomedical issues. At the same time, in so doing, the products of these interventions (to administer the chemotherapy) become part of the phenomenon they are monitoring (patient's response to the chemotherapy). It is relevant to acknowledge that this can produce contradictory consequences or complex issues to be solved. On one hand, clinical technologies for performing the trial can force convergence around standards; on the other hand, contingent solutions to make concerned technologies at work (e.g. clock synchronization) can introduce contextual serendipity that surfaces as randomness at other times and in other places (e.g. when collecting blood samples at the bedside).

This implies negotiations across diverse professionals that may occur via specific organizational arrangements. Thus, we can observe cancer precision medicine as a context dense with (organizational) indeterminacies, which must be addressed as "going concerns" (Rip and Joly 2012) to be managed and normalized in the clinical setting. In this case, coordination between the clinical team (especially the nurses) and the laboratory staff is crucial for the collection of blood samples, of data on blood sampling and of patient responses to the trial. This may produce some tension between professionals engaged in the trial, since its execution involves practices interacting within a broader network, such as communication between the oncologists and the hospital pharmacy, which can also generate errors. Or even coordination between the laboratory staff in charge of conducting the pharmacokinetics study of the samples and the research nurses who must collect blood samples in compliance with the protocol in order to minimize contingent errors and to preserve data collection integrity and reliability.

Knowing – in the form of professional participation in a clinical trial designed to validate a novel precise therapeutic option – is not confined to a single setting and a local epistemic community but is interwoven with a web of epistemic practices. In such a context, the experimental pharmacologist constantly refers to the implications of protocol rules in guiding her experimental actions. In this respect, compliance with the rules implies interaction with other organizational rules. Indeed, the pharmacologist, in doing her job, uses not only propositional knowledge but also her experiential and detailed knowledge (her know-how of how nurses, the

hospital pharmacy and oncologists work) to achieve the effects expected of following the protocol – namely, to render blood sampling procedures technically reliable to explore interaction patterns between the genotype and the chemotherapy regimen within a given disease. In other words, the pharmacologist demonstrates a highly pragmatic approach to the application of rules, guided by the need to find a solution to the situation at hand that is feasible (it works), acceptable (it produces a reliable sample) and epistemologically adequate (it upholds the integrity of the protocol).

The biological sample is constructed in such a way that it becomes the material mediator of the disease under investigation between the clinic and the laboratory. The latter, far from being in a relation of otherness with the clinic, contributes to building the patient's bio-clinical trajectory on which clinical interventions are informed by a rationale that is not purely therapeutic. Thus, by moving between the clinic and the laboratory, Pina locates the disease/body under experimentation in a boundary space to ensure that the collection of biological samples is carried out according to the protocol's standardized indications. The relation generation of a boundary space is the effect of articulation work (e.g. asking the patient what time the sample was taken; see Strauss 1993), which is necessary to ensure precise practices to generate precise knowledge. Generally speaking, articulation practices are a kind of cooperative work to facilitate trial work. Indeed, the mobilization of different expertise and technologies, in their nature and in their purposes (sometimes ambivalent), in trial work implies a need for articulations due to the interprofessional dynamics and changing situation in respect to collective aspects. In this regard, articulation work implies inter-laboratory iterative negotiations involving various professional communities within and between different settings informed by distinctive logics of acting. In this sense, the organizing context of action in precision medicine is multiple and heterogeneous, as it can be the patient's body, the laboratory (with its instruments and rules) or the clinic. To shape the organizing context in which to locate precision practices, professionals are required to learn how to stress both similarities among diverse settings (e.g. the clinic and the laboratory are working for the patient's benefit) and differences across institutional boundaries (e.g. the laboratory requires specific standards to manage the body). From this perspective, articulation work is materially mediated by mundane objects, biological materials and technologies to infuse therapy and to shape congruency between spaces informed by different epistemological regimens, moral assumptions and professional cultures.

4. Discussion and concluding thoughts

This paper has considered the ways in which clinical and laboratory practices are closely interwoven in the context of genomic-informed clinical trials and how their respective fields can be reshuffled, although they might have an internal epistemic structure. The relationship between the diverse organizational sites and

related knowledge-brokering mechanisms has important implications for research in the area of (bio)knowledge production, highlighting that no single organizing strategy may suit all knowledge translation circumstances. In this regard, even when engaged professional communities work ostensibly within the same genomic-informed trial, they may achieve precision knowledge translation in different ways. Thus, the presented ethnographic episodes are useful for determining, from the outset of a concerned trial, how both knowledge-brokering dynamics and articulation work may operate within a particular bio-clinical network.

In so doing, the paper has framed the production of precise (bio)knowledge as a bio-clinical texture to disclose how relations (socio-technical connections between human agents, organizational settings and artefacts) come about and are established, thereby emphasizing how practitioners work together to enact precision knowledge. Instead of assuming a taken-for-granted concept of precision medicine, this study focussed on healthcare professionals and laboratory workers and entailed observing their everyday practical accomplishments required to define personalized cancer therapy. Accordingly, the study adopted a perspective oriented towards disclosing the organizational arrangements, expertise, technologies and activities involved in practical and situational fabrications of actionable, precise knowledge. Here, precision knowledge-making procedures were analytically captured as an open-ended process requiring heterogeneous abilities to move across various care and research settings and time frames as well as to respond to different privileged epistemic regimens. In this sense, organizational arrangements and work practices are closely interwoven, and the interconnections between knowledge, practitioners and technologies constitute the bio-clinical network to enact the precision clinic, which the social researcher can explore without needing to postulate aprioristic differences among epistemic regimens or levels of knowing (Gherardi 2008).

Concerning laboratory-based and clinical professionals, different identities and practices are shaped and come with different ways of performing precision medicine, just as the practices through which the precision clinic is performed are multivarious and informed by different epistemologies, professional values, orientations and practical objectives. The findings show that precision medicine is situated within a choreography of bio-clinical practices acting in hybrid spaces where molecular and clinical developments align. Barriers between care and laboratory settings simultaneously constrain and generate precision practices, thereby shaping the organization of everyday work in situ. This is marked by a plurality of actors, technological objects and privileged epistemic regimens comprising ideas, projects and emotions that human agents assign to their organizational behaviors to locate precision medicine in specific socio-technical settings in which precise knowledge is enacted as a form of knowing in practice. Indeed, precision medicine is a matter of practically defining *what is precise*. It neither exists before the beginning of a trial to test a new therapeutic option nor when it is evoked in institutional documents. It is only after it is performed through practices

that the precision clinic is shaped and shapes precision itself. This is a crucial point, and it is especially so for uderstading clinical trialists work. Their purpose is to establish not only new standards of treatment and care but also, as has been underlined, a standard concerning how to be "precise", or rather, how to organize settings that allow for rendering precision knowledge clinically actionable. From this viewpoint, the notion of knowing in practice helps to define the field of precision medicine as a context in which the concrete activity of producing and using (bio) knowledge becomes visible and observable, as well as describable, without assuming an external concept that pervades the field under scrutiny from without. Theoretically speaking, the findings suggest that neither boundaries nor relations mark the difference between biomedical spaces. Instead, boundaries appear, at times allowing leakage, and disappear while relations undergo a transformation in terms of knowing how to know precisely.

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Notes

1. The article employs the term "(bio)knowledge" descriptively. It encompasses all those specific practices and expertise occurring in the context of clinical trials in cancer precision medicine that configure the knowledge-making process concerning the clinical and biological existence of cancer patients both in their molar (see Rose 2007) and molecular dimensions.
2. A single nucleotide polymorphism is a DNA sequence variation of a gene – here, the "UGT1A1" gene.
3. The HPLC is a technique adopted by laboratory staff to study the metabolism of drugs administered within a Phase 1 genomic-driven clinical trial aimed at personalizing treatment for patients presenting colorectal cancer.
4. This is the blood sample used in pharmacokinetic studies conducted within phase 1 clinical trials, allowing for quantifying the maximum concentration of the administered drug(Cmax).

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