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Perspective

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Regenerative Medicine

Regenerative medicine and responsible research and innovation: proposals for a responsible acceleration to the clinic

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This paper asks how regenerative medicine can be examined through the 'responsible research and innovation' (RRI) approach which has been developed over the past decade. It describes the drivers to the development of RRI, and then argues for the need to understand innovation itself through drawing on social science analysis rooted in science and technology studies. The paper then identifies a number of highly specific challenges faced by the regenerative medicine field and the implications these have for value creation. It offers a number of examples of how a combined RRI/science and technology studies perspective can identify priority areas for policy and concludes by arguing for a 'responsible acceleration', more likely to foster readiness at a time when much of the policy domain is pushing for ever-rapid access to cell therapies.

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The field of regenerative medicine is progressing as both a scientific and clinical endeavor, on a variety of fronts. It is a heterogeneous field whose boundaries can be contested [1], one that is both complex and novel, not least as it is outside of the conventional domains of drug or medical device-based medicine, dependent instead on the derivation and manipulation of different forms of tissue for therapeutic, perhaps even curative, application [2]. It is this very novelty that has led to commentary [3] on its specificity as a field compared with other innovative biomedical areas such as robotics or digital health, and associated calls for bespoke forms of evaluation and regulation more suited to it [4]. Moreover, as an emergent field with much promise, the hype and hope surrounding it has been captured by commercial organizations keen to exploit its potential [5,6]. In some countries concerns over 'unproven' therapies have led to calls for much tighter regulation of this rapidly growing market, as McLean *et al.* [7] have argued in regard to Australia.

Novel fields of inquiry and practice outside of the field of regenerative medicine, and the complexities and attendant uncertainties and concerns that surround them, have often been the focus of debate among bioethicists [8] political scientists [9] and sociologists of science [10–12] as well as those directly involved in trying to both promote yet oversee safe innovation [13–15]. Within this wider context, we have seen the development over the past 5 years of a new paradigm through which to understand and both enable yet constrain emergent science and technologies that are shot through with uncertainty and novel risk; this is the move toward the paradigm of 'responsible research and innovation' or 'RRI'.

Responsible research & innovation

Having its initial roots in work on nanotechnology [16] but given considerable impetus thereafter by the European Commission [17], the influence and application of RRI have grown rapidly [18]. Indeed, the Commission's Horizon 2020 program has a strong RRI focus as a core element running through it, calling for research which produces innovation that is ethically acceptable, sustainable and socially desirable [17]. We can see similar turns to RRI at a national level. For example, in the UK, the joint EPSRC/BBSRC [19] synthetic biology/bioengineering program has developed an RRI governance model for those projects it funds, and thereby shapes in a quite specific way.

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Elsewhere, the CSIRO in Australia has a new 'SynBio' program *"built on a philosophy of responsible development of synthetic biology technology, striving for ethical outcomes and working within the bounds of social acceptance"* [20]. Similar developments can be found in the USA and Denmark [21] while calls are made for RRI to be introduced elsewhere, where opportunities to do so may prevail and where an RRI intervention is timely, such as in the current Brazilian innovation context [22].

It is, then, important to ask what are the main drivers behind the development of RRI? An early version of RRI came in the form of the 2003 International Dialogue on Responsible Innovation initiative taken by the USA and the EU to address growing concerns about nanotechnology, following in the wake of the controversy over genetically modified organisms, and the desire to avoid a similar one in nanotechnology. Nanotechnology was a key site for debate because of concerns over 'nanoparticles' [23]. Though its origins lie in nanotechnology, the work of Robinson and others developed the concept to help address the complexities and risks inherent in any emergent field, as part of a wider program of work on 'future-oriented technology assessment' and the related 'constructive technology assessment' [24].

There are perhaps four drivers that have shaped the RRI approach. The first (as in the nanotech case) is simply that the impact of any new technology is difficult if not impossible to predict. This is not simply in terms of its relationship to other technologies or a specific market for innovation, but because all technologies have both intended and unintended effects not least, and perhaps most important of all, in regard to their impact on social relations. As Barry [25] argued most convincingly a number of years ago, the novelty of a technology lies as much in what new social relations it creates as it does any technical innovation *per se*. As a recent paper by the Dutch Rathenau Institute [26] observed, *"Digitalization does not simply transform existing practices into digital ones; it creates new practices"* (page 13).

A second reason we can include here relates to the ways in which science itself has become more reflexive of its own activity, where societal questions are not on the outside but fundamental to science itself. This has been characterized as the recontextualization of science, that is science more aware of the context within which it is produced, and thereby a greater preparedness for caution and to embrace uncertainty [27].

A third driver is that early societal intervention may enable both the positive and negative impacts of innovation to be anticipated. This is not though simply in terms of possible risks – such as the environmental concerns over controlling nanoparticles – but much broader considerations over the governance of innovation itself – the direction of travel it might take, how this may become locked-in and eventually counter to what was envisaged, and so on.

Finally, and an extension of this last point, RRI can be associated with a more macroeconomic critique of the ways in which an 'innovation-at-all-costs' seems to dominate science and technology policy in most neoliberal states and in particular the new bioeconomy [28,29]. Against this view, writers such as Mazzucato [30] have called for a move away from a concern with the rate of innovation (measured for example in terms of gross domestic product) toward a concern with the direction of travel it has, and indeed calls for a different innovation register altogether, even one that embraces 'responsible stagnation' [31].

Development of the RRI perspective gained particular momentum when a broad theoretical framework for it was developed by Stilgoe *et al.* [32] in a seminal paper that articulated its core propositions. These are that RRI is characterized as an approach to innovation guided by four principles, those of anticipation, reflexivity, inclusion and responsiveness [33]. These four principles can be outlined as follows: anticipation refers to an approach toward scientific and technological innovation that offers a robust analysis of possible risks as well as opportunities that may lie ahead, recognizing the contingencies involved here; reflexivity requires an openness and transparency in innovation policy and practice that acknowledges the competing values and contested nature of innovation, an approach that should inform all levels of governance (including the formal regulation) of science; inclusion takes this further by ensuring that different voices are included in the governance of science, requiring diverse forms of public engagement and dialogue and; responsiveness means establishing a set of procedures that can enable response to changing circumstances, and ensuring these procedures are in place ahead of decisions that are typically made (about future development) under some conditions of ignorance. The paper by Stilgoe *et al.* operationalizes these broad principles in terms of a series of more specific questions that they prompt, questions that are related to the product, process and purpose of any specific innovation. For example, in terms of a product, how will its risks and benefits be distributed; in terms of process, how might such risks be measured and by whom; and in terms of purpose, could there be an alternative way toward achieving the desired innovation objective? More broadly, we can understand RRI as being about both future-oriented 'care and responsiveness' and backward-looking 'liability and accountability' [34].

I shall return to these ideas in more empirical terms when asking how they would inform the field of regenerative medicine, and so what an RRI-driven approach would look like. Before doing so, it is equally important to consider the term 'innovation' itself, but here less from an RRI perspective, and rather from the disciplinary approach known as science and technology studies (STS). Work in STS stretching back over many years has demonstrated the nonlinear, complex and messy process of innovation, and importantly how the relationship between producer and user is recursive: as Hyysalo *et al.* [35] argue, *"STS. . . [has] a deep understanding of the contingent and interactive innovation processes. . . [that] is never an insulated, autonomous process that develops according to its own logic"* (page 19). As a result, STS begins with a set of assumptions far removed from conventional linear, 'technology-readiness' narratives seen in much of the innovation policy and business studies literature. While the commentary from RRI above helps to identify important substantive ways in which innovation can be more 'responsible' or 'responsive', an STS perspective argues that all innovation paths have diverse, often competing possibilities, and any settled innovation could have been otherwise. This immediately opens the door to asking the very same questions voiced by RRI, but now from a '*theoretical*' rather than '*normative*' perspective.

Two central points can then be made: the recursive relations between producer and user of novel innovation mean that markets have to be built, rather than as often seen as 'innovative technologies' looking for a solution. As Callon [36] has argued, using the analogy of the Scrabble board: *"A market is like a Scrabble board: there is no point in wanting to place an innovation that does not correspond to the possibilities it affords . . . no point in keeping aside the perfect word"* (page 82). The innovation may need to be redesigned, broken up, repurposed to find an innovation space ready to receive it. Of course, unlike a Scrabble Board, in real life it is possible to create some new spaces (at the side of the board, as it were) to provide niches or safe-havens for emergent technologies. But this is difficult and clearly a challenging social, or better a sociotechnical process, and never simply a 'technical' matter [37]. I shall return to how such niches have been created for regenerative medicine later on.

The corollary to this is that the take-up and implementation of new technologies depends on their being not simply technically 'working' in the sense that they function to serve a particular designed purpose, but that they are 'workable' in contexts. Moreover, context itself is not a static, pregiven state of affairs, but moving, processual and a reflection of the interplay of old and new relationships and practices which together stir an innovation to workable life [38].

We can now turn our attention to regenerative medicine and examine its innovation space and characteristics. The paper explores the particular innovation challenges it faces – what sort of Scrabble board it confronts – and the sense in which these are peculiar to the field, that is, unlikely to be found elsewhere, and the response made by government and other actors to this. I argue from an RRI perspective that these only take us so far. I go on to outline what might then be an STS-informed approach to regenerative medicine which can take us further and which is shaped by the four normative prescriptions of RRI.

Regenerative medicine: challenges in creating innovation value

There are high expectations as to the impact that regenerative medicine will have in healthcare systems. It is envisaged that it will provide much needed treatment options, including curative treatments, for a range of ailments for which there is currently a high unmet clinical need and from an economic perspective regenerative medicine has been framed as a driver of future economic growth. The UK government, for example, has identified the area as one of 'eight great technologies' which will generate significant economic prosperity and in which the UK can become a global leader, and similar pronouncements can be found elsewhere [39]. There is also much made of the rapid increase in investment in the field (despite few products actually on the market) [40].

Given these expectations and scale of investment, where might value – both in its commercial and clinical forms – be found in the field? Figure 1 summarizes the different domains where value might be added and so extracted by different players. These values can be both of a monetary form or knowledge-based (new scientific understanding, new forms of evidence and data, etc.). Each of the four columns offer possibilities on both fronts: for example, companies might specialize in providing specific derivation (column 1) or extraction (column 2) services while in each there are also valuable forms of bioclinical knowledge to be derived. For simplicity sake in the diagram, the links move to the right, but there is also a recursive relation between the four: for example, research and development in the area of gene therapy (showing a particularly rapid growth today) can help inform the way in which cell line characterization is undertaken in respect to securing relevant genetic information needed for 'clinical grade' lines.

The rather schematic diagram of the field seen in Figure 1, though helpful in seeing potential sites for value generation, says nothing about the actual challenges that this brings. These are summarized in Box 1. Primarily,

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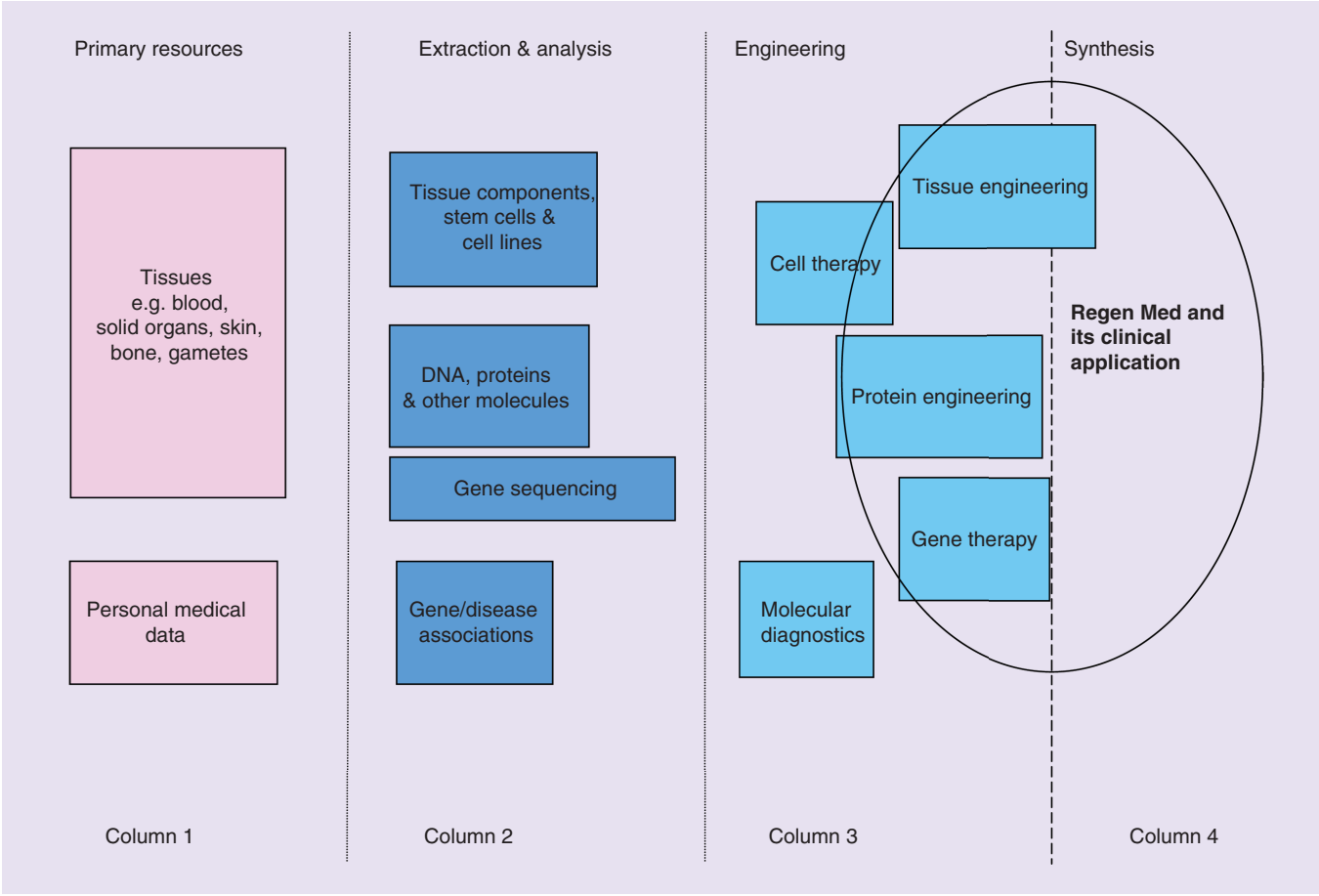

Figure 1. Different areas where commercial/clinical 'values' might be added/extracted.

Box 1. Challenges relating to realising innovation value in regenerative medicine†.

Clinical trials
- Complex environment overseen by multiple bodies
- Uncertainties & risks associated with the use of live tissue
- Inappropriate clinical trials design and costing templates

Regulation
- Burden of many relevant legal provisions
- Heterogeneity in implementation of provisions across different countries
- Major difficulties associated with the classification of different Regenerative Medicine products

Manufacturing/scale-up
- Underdeveloped infrastructure for scale-up and transport to the clinic
- Lack of consensus regarding quality assurance of tissue
- Lack of suitable qualified persons at clinical sites to oversee and approve proposed treatment

†Data taken from [41].

they relate to the nature of this form of 'medicine': its anchorage in the sourcing and manipulation of live tissue and cells, a very different challenge from that found in the biochemical or biomechanical worlds of drugs and devices. It was this difference that led to the development in Europe of the Advanced Therapy Medicinal Products classification scheme through which thereafter regulatory approval for regenerative medicine products might be given.

As these issues have been discussed elsewhere [41], here we can rehearse some of the arguments related to a few rather than all the points made in Box 1. Thus, in regard to clinical trials, it is well known that there are

particular safety and efficacy challenges deriving from the perceived complexity and fragility of live material used in early Phase trials. Moreover, the use – found throughout conventional trials – of surrogate end points (laboratory or physiological measures used to predict or provide an early measure of therapeutic effect) has been seen to be inappropriate in trials where real clinical end points are needed; in addition, large-scale randomized controlled trials are also unlikely especially where small populations (especially in rare disease areas) mean that the usual convention of recruitment to trials with two treatment arms would require many centers, much time and great expense.

In regard to manufacturing and scale-up, although scale-up, quality assurance and related issues are seen in many novel applications outside of regenerative medicine, they are particularly difficult for regenerative medicine products which are based on living tissues and cells. Unlike mass production of drugs, cells are live tissue, so generating (many trillions of) cells for clinical application at standard quality levels is difficult: the growing environment can affect the safety and potency of the material while the shelf-life may be as little as a few hours; the inherent variability within cell lines means that the 'chemicals'-based concept of 100% 'product purity' and reproducibility may not be possible; the manufacturing of most products must take place within a clinical-grade GMP-licensed facility; and finally, given that the 'shelf life' of this material is very limited, either a decentralized, distributed 'bed-side' closed system manufacturing models will be likely, using automated, modular, closed-system manufacturing platforms or a series of microfactories providing just-in-time provision of cells to patients will need to be built [42]. This, in turn, will create new demands and tasks for hospitals themselves for they will have to act as both the site of procurement of starting materials (cells and tissues) and also the delivery of final product to the patient and may even be likely to become active in the partial or full manufacturing of the product itself.

In light of the above, it would be reasonable to propose that an RRI approach to regenerative medicine should at least consider these three particular challenges – the trials process, the classification/regulatory process and the scale-up process and how they might be addressed. These mark out the territory on which RRI engagement might be found.

Indeed, those responsible for policy, for regulation and for the economic evaluation of the field have expended considerable effort as well as material and financial resources to respond to these concerns. The specificity of regenerative medicine has, across many countries, led to diverse government and other initiatives to help regenerative medicine get to the clinic. However, the current strategy is not based on RRI but on a conventional linear approach – in particular one framed by a preoccupation with accelerating regenerative medicine's technological readiness for the market – and so its commercial and clinical value. The approach taken is very much premised on the notion of ensuring a technological readiness that can then be pulled through to the market and full adoption. This is to focus on innovation as 'working' but gives less attention to a sociotechnical exploration of the contexts in which it will become 'workable'. It is, for example, clearly crucial to make every effort to undertake quality assurance tests on cell lines prior to their being made available for clinical trials, and to the extent that the lines meet the testing criteria they are 'ready' and working. However, they will only become workable as such if they make sense in their context of application – the specific challenges – including professional and patient concerns – within the clinic.

Ironically, the various ways in which key actors are trying to accelerate – in other words, to reduce – time taken to the clinic, has actually brought to the fore this problem of workability, ironic inasmuch as in doing so the organizational and institutional issues that arise raise new questions that slow the process down. This, in turn, leads to new policy initiatives that are designed to speed up the process again.

We can see this, for example, in the case of the UK's very recent, and more broadly-based, initiative to develop an accelerated access model for innovation across the board within the NHS – to identify, capture and nurture that innovation. Similar measures are being taken in the USA, in Europe and in Southeast Asia. In regard to the UK, concerns over the stalling of innovation led to plans toward the end of 2016 for accelerated access via a new 'Accelerated Access Partnership' (AAP), made up of a large and diverse range of stakeholders (see Figure 2), who will be responsible for identifying innovations that can be given a 'transformative designation'.

The proposal is that the AAP will seek to identify a core of between 5–10 products each year (from a larger universe numbering c.50) that will receive this designation, chosen for their 'clear and measurable outcomes', 'alignment with NHS priorities' and demonstrably quicker pace to the clinic precisely through the AAP's intervention. Going back to the Scrabble board analogy, the AAP has to create through a collective (rather than individual player) endeavor a new space within which these products can be located and given value. The especially notable aspect of the AAP is that *the partnership itself* can be seen as transformative as the products: this will be a novel and challenging cooperation to make the products workable. As such, it is likely to demand the marshalling of different forms of evidence, different interests, different infrastructures (commercial, regulatory and clinical) and in doing so

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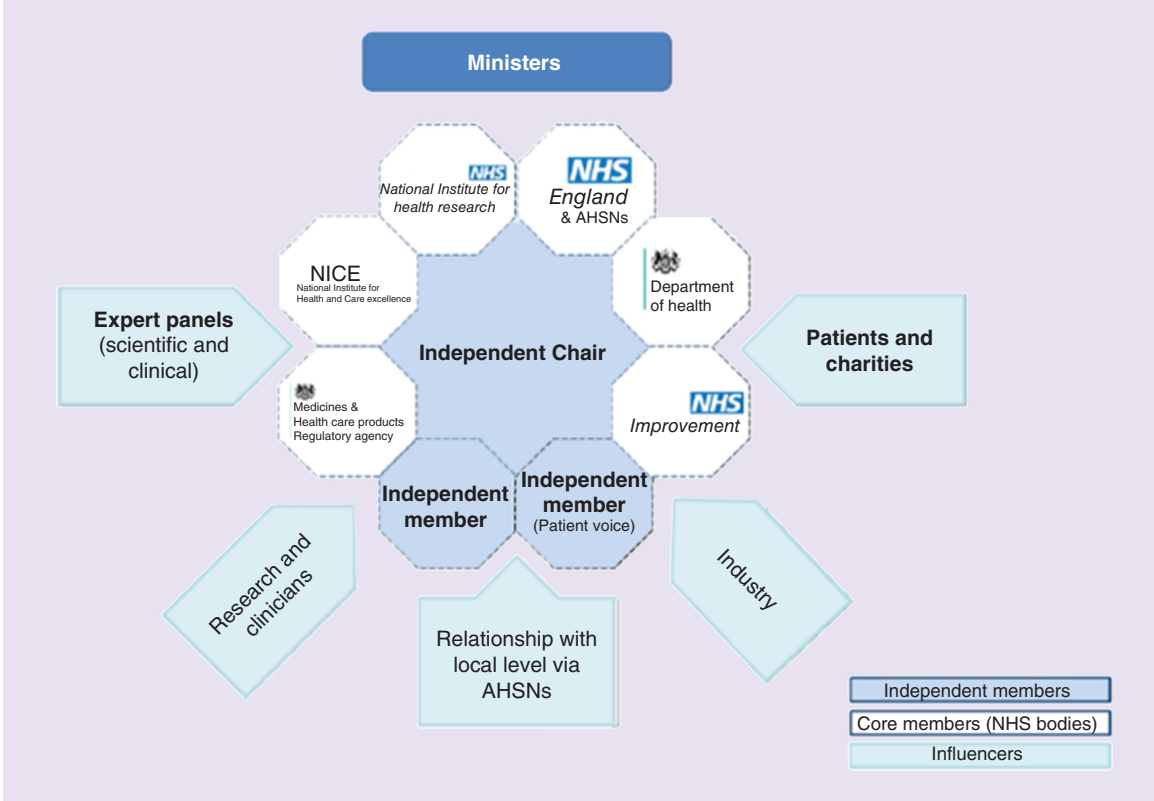

Figure 2. The accelerated access partnership.
AHSN: Academic Health Science Networks.
Figure taken with permission from [43]. Contains public sector information licensed under the Open Government Licence v3.0.

make visible and have to resolve different existing priorities (over budgets, commissioning, skills base-needs, and so on). In other words, accelerating access is likely to require a considered and careful transorganizational engagement, unlikely to happen properly at speed. What emerges from this will be a welcome explicit understanding of the ecology of innovation and the making visible of what is often hidden [44].

In short, what this suggests is that we need to focus on what we can call *institutional* (and not simply technological) readiness, that is, the work needed to understand the adoption of innovation in specific contexts. Paradoxically this embraces unreadiness – a recognition of a heavy uncertainty overhead involved in facilitating innovation, and a slowing down to enable what we can call socially robust innovation [45].

Often in these situations, policy looks to see whether there are models, comparators, elsewhere that might facilitate this process and so foster workability. One such model in the UK and possibly elsewhere is that of the NHS' Blood and Transplant (NHSBT) service which for many years has sourced and supplied to quality-assured level's blood products to hospital sites. Not surprisingly, the NHSBT has been identified by the Cell and Gene Therapy Catapult (whose very name suggests acceleration) as not only a good model but actual recruit to assist in the move to the clinic [40]. Whether the NHSBT will play a role in the AAP is not yet clear (they do not figure in the diagrammatic map at this point in time). But as a recent Catapult-led report notes, the *"NHSBT has worked with the Catapult to determine how its cell therapy infrastructure could be utilized to support the logistical aspects (i.e., movement, manipulation, final preparation and storage) of various types of cell therapy products from their site of origin to UK hospitals"* [40]. Working with the existing institutional grain and lesson-learning from elsewhere [46] makes for a speedier and yet robust development process.

Regenerative medicine & responsible innovation

I now turn to ask what an RRI perspective on regenerative medicine might look like. It will not only want to ensure that workability as sketched out above is possible, but do so on specific terms. In other words, it will ask the sort of

Box 2. RRI and its role in regenerative medicine.

Anticipation
- Need to develop scenarios based on discrete population groups and disease areas – model this in terms of resources and skills needed and scale-up with best use of scarce resources at regional/national levels

Reflexivity
- Develop new methodologies relating to cost and benefit that consider a continuum of care beyond the initial therapy

Inclusiveness
- Data collection via clinical studies and trials – not just evidence-based medicine (the CT) but medicine-based evidence – patient centered and attentive to patients' valuations of and control over different therapeutic interventions

Responsiveness
- Transparent governance across companies, regulators, patient groups, clinicians; especially important in 'risk-sharing' schemes and the knock-on effect these have on trials as such

questions noted much earlier in the paper – how will the risks and benefits of regenerative medicine be measured and distributed and are there alternative ways in which the field might develop? Applying the four core features of RRI, what practices need to complement the development of working technologies to make it possible to manage uncertainty and so make the technologies not simply working but workable – how can we help build 'institutional readiness'?

Box 2 offers a number of ways in which we can operationalize the four principles of RRI to the regenerative medicine field. They also reflect the three concerns noted earlier in the paper relating to trials, scale up and regulation. In the case of 'anticipation', it will be important to undertake forward-looking analyses of the way in which the field can address the different needs of discrete population groups by disease area and location. This will also need to be done in light of the heterogeneity of the field: as Ginty *et al.* [47] notes, *"there is a 'diversity of cell types, disease indications and delivery pathways' that makes a 'once-size-fits-all manufacturing platform unlikely"* (page 245). The field has inevitably developed unevenly partly a reflection of the challenge in the science base and partly as a reflection of the existing centers of research and clinical excellence that tend to concentrate in major metropolitan areas, such as the so-called 'golden triangle' of Oxford, Cambridge and London in the south east of the UK or the equivalent in Massachusetts, California or Canada (notably Toronto, Quebec and Montreal) in North America. To date, what we might call the geoclinical availability of regenerative medicine has yet to be modeled. In addition there will need to be anticipatory work undertaken to develop robust models of treatment centers that can be configured in such a way as to meet the range of challenges described above. Aligning and integrating the existing infrastructural capacity (as displayed by the NHSBT) with specialist centers will require careful understanding of the resources and skills-base that are needed and where responsibility for key elements of the production, delivery and use of cell therapies will lie. In regard to reflexivity, a particular emphasis should be given to the need to be reflexive about the assumptions that underpin clinical trials design that have been driven primarily by a pharmaceutical model. Here, an RRI approach would attend in particular to some of the core scientific uncertainties that characterize cell therapy trials, relating for example to biomarkers and end points, and in clinical terms, variability in patient response [48]; what sort of clinical trials design makes most sense in this context [49] and how can future trials design and its regulatory oversight accommodate this?

The question of inclusiveness is perhaps best considered in regard to what sort of evidence and data are included in determining the contribution that the field can make? Typically, this has focused on the measures used within evidence-based medicine (EBM) even though these have been subject to criticism in other fields of medicine. Most relevant here is the observation that the *"inflexible rules and technology driven prompts (of EBM) may produce care that is management driven rather than patient centered"* [50]. Even if it is important to retain EBM, its focus primarily on statistical data and analysis is far removed from medicine-based evidence, that is, evidence that is of equal importance when moving toward a more patient-centered regenerative medicine. This is not just about garnering interpretive data but more significantly from an RRI perspective enabling patients and patient representatives (especially patient charities) to actively engage with the medicines development process and help determine what sort of agenda and measures should be used in the development of new products. We can see attempts to do this in a systematic way through for example, the Critical Path Institute in the USA, which is working with patient charities and industry globally to develop a more patient-centric model of medicines development in a diverse range

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of disease areas and, in turn, rethinking the clinical trials design, particularly in regard to pooling precompetitive data [51,52].

Finally, in regard to responsiveness, this element of the RRI model is primarily about ensuring appropriate governance and regulation models. Here the focus should be on ensuring such models are understood and subject to critique and debate: while this has characterized medical governance for many years, in the context of regenerative medicine a key focus should be on the turn toward risk-sharing models which are part of the 'accelerated' pathway to the clinic, giving patients early access to medicine while reimbursement is provided gradually depending on the outcome of treatment over time. Such an approach was explored and recommended for consideration in the UK's Regenerative Medicine Expert Group report on 2016 [14]. Key here is how evidence about treatment is secured and measured and how this then translates into an (emergent) value for the product itself. An RRI perspective would seek to ensure that risk-sharing while enabling early access for patients does not generate more uncertainties than already exist in regard to clinical evidence or trials data. In fact, it is worth noting here – echoing a general point already made – that risk sharing, ostensibly about enabling a quickening of access to the market, generates new uncertainties which can disincentives companies from taking up this opportunity, and so may paradoxically slow things down [53].

What this discussion of how RRI might play a role in the field suggests is that there are important ways in which an RRI approach will help enable institutional readiness, and overcome the incommensurability between existing healthcare delivery mechanisms which have emerged to support drug and device-based therapies, and the particular requirements of tissue, cell or gene-based regenerative medicine products. The examples given in Box 2 are not exhaustive; it would be possible to develop additional arguments centered on the four core concepts. For example, it will be vital to explore how hospitals might become sites of both the production and use of cell therapies, not inconceivable in a distributed model of development [54], and what capacity they have to do this and at what cost.

Conclusion: responsible acceleration

This paper has argued for a combination of RRI and STS approaches to offer an improved understanding of how the innovation paths that will best deliver regenerative medicine to the clinic can be given a distinctive shape and direction. The turn toward the language of acceleration has been discussed and shown to be in need of much fuller consideration of what has been called institutional readiness. Much of the commentary on acceleration has been about providing access to 'medicines', as though the latter was in some way self-explanatory or simply a 'therapeutic product': medicine as such is a complex set of social and clinical processes that give the context within which a therapy is deployed and given meaning. This implies that a specific 'medicine' may in fact have a variety of identities and given purposes as one moves from one context to another. This has important implications for the complaint often made by government that good innovation is unevenly adopted and barriers must be lowered. Rather than the language of barriers it would be better to see what relationships need to be mobilized to make novel medicines workable. In making them workable, complexity as such is not completely removed; instead, some agreement can be made about how it can be handled, and to what degree some simplification of it as doable can be agreed [55].

Second, the RRI commentary suggests that we should be prepared to slow down at times [56], to move toward what we might call a 'responsible acceleration' precisely in recognition of the fact that robust forms of novel medicine depend on robust forms of social organization and partnership. The AAP is in principle an excellent vehicle for this but will require considerable work on developing a co-production approach to the designation of 'transformative' medicines, including those in the regenerative medicine field.

Finally, these arguments are timely inasmuch as in the UK government and the Department of Health are considering proposals for the development of Advanced Therapy Treatment Centers [57]. These are not the 'centers of excellence' which, as upstream science-based organizations populate most national landscapes, but centers where treatment is to be given to patients. To do this properly will require as much investment in new forms of social and clinical organization as it will in the biomedical infrastructure on which it will depend.

Future perspective

While the paper has discussed a range of challenges associated with the development of regenerative medicine, the very specific nature that these have actually means that handling the complex challenges that are thrown up should make the field especially suited to embracing RRI. Conventional linear approaches to innovation development and adoption are of limited value when the product is the process and where we need to rethink how that process can be introduced into existing clinical delivery and wider healthcare systems. Providing the right sort of organizational

and scientific infrastructure for regenerative medicine is vital. There needs to be a paradigm-shift away from a traditional approach to product development to one that focuses on a more coordinated value-chain, on targeted (rather than broad) population groups, patient access and on a broader range of evidentiary sources to track and assess emergent therapies. 'Transformative' products are in fact transformative processes in this field, which then need a transformative organizational and institutional framework to support them. Such a framework can be made more effective and robust if it were to embrace the four principles of RRI.

The likelihood of doing this over the next 5 years will depend as much on senior policy advisors and regulatory agencies working together with hospitals, patients and clinical and social-science researchers to build new bespoke centers that are responsive to unforeseen developments as therapies become more established and yet require new forms of clinical monitoring.

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Executive summary

- The field of regenerative medicine is progressing as both a scientific and clinical endeavor, one that is both complex and novel. Within this wider context the move toward the paradigm of 'responsible research and innovation' (RRI) can help understand and manage such complexity.

Responsible research & innovation

- The responsible research and innovation approach has developed rapidly over recent years across diverse national and international contexts, reflecting the potentially transformative yet uncertain promise of science.
- As a paradigm for scientific innovation it is based on the principles of anticipation, reflexivity, inclusiveness and responsiveness.
- A science and technology studies perspective can bring added analytical insight to the meaning of innovation and should be brought to bear on the RRI approach.

Regenerative medicine: challenges in creating innovation value

- There are potential sources of value in regenerative medicine, though these will depend on recognizing the specific features of the field that differ considerably from conventional medicine.
- These features relate in particular to the trials process, the classification/regulatory process and the scale-up process.
- We need to move from an approach to innovation that is driven by a technological readiness perspective to one that has a broader basis *viz.* that of an institutional readiness, emphasizing the move from a technical working to a contextually workable clinical innovation.

Regenerative medicine & responsible innovation

- The four principles of RRI can be applied to regenerative medicine to throw into relief-specific areas for RRI-informed practice and planning that recognizes the special demands the field will have in moving to the clinic. A number of examples are given.
- This RRI approach allied to the science and technology studies perspective will help enable institutional readiness, and overcome the incommensurability between existing healthcare delivery mechanisms which have emerged to support drug and device-based therapies

Conclusion

- We need to move toward what we might call a 'responsible acceleration' precisely in recognition of the fact that robust forms of novel medicine depend on robust forms of social organization, new skills and new forms of partnership.

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