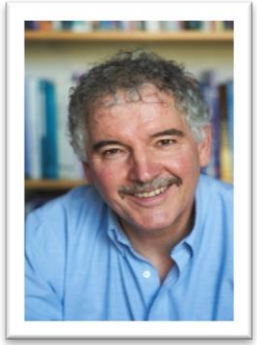

Workshop Session

Institutional Readiness for Advanced Therapies

Prof. Andrew Webster

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Advanced Therapies Treatment Centre

Institutional Readiness for Advanced Therapies
Professor Andrew Webster, SATSU, University of York, UK.

NAATTC Conference

Reflections on Advanced Therapy Delivery in the NHS

May 21 2019

Outline of presentation:

1. Context and the specificity of regenerative medicine
2. The concept of institutional readiness
3. The Advanced Therapy Treatment Centres
4. Conclusion and implications for the NAATTC

1. The broad context

1. Some key S&T developments in regen med as a field
CRISPR and CAR T-cells – rapid increase in scientific/commercial activity
Major increase in iPSC activity and recent trials in Japan (e.g. March 2019 corneal tissue produced from iPScells)
Release of UKSCB clinical grade lines
8 ATMPs approved by EMA – though with variable success
Moves to merge health informatics and cell production – new bio-platforms
Increasing interest in sharing clinical data peer-to-peer and enabling a new way of integrating large discrete data sets
Responding to immunogenicity: towards an iPSC haplobank
Regenerative therapy to restore function paralleled by move towards preventing *de*generative structures in first place

Main areas of activity

1. *Enabling, gateway innovation such as immunotherapy: e.g.* gene-modified CAR T-Cells for leukaemia [e.g. Oxford Biomedica]
2. *Automated cell processing 'point-of-care' device/technique*: e.g. the 'Celution System' [Cytori - Deeside]
3. *Surgeon-led innovation* – e.g. the bioengineered trachea [Videregen/UCL]
4. *Implantation/infusion therapy innovation:* e.g. wound/skin repair (which would not occur naturally) [Tissue Regenix - Leeds]
5. *Bioprocessing innovation* - e.g. expertise and services to other parties [Cellular Therapeutics - Manchester]

Total Clinical Trials by Technology Type as of EOY 2018

Alliance for Regenerative Medicine

Gene Therapy

Total: 362
Phase I: 120
Phase II: 210
Phase III: 32

Gene-Modified Cell Therapy

Total: 362
Phase I: 158
Phase II: 188
Phase III: 16

Cell Therapy

Total: 263
Phase I: 53
Phase II: 177
Phase III: 33

Tissue Engineering

Total: 41
Phase I: 10
Phase II: 20
Phase III: 11

Source data provided by: informa

Have to recognise *specific* context within which RM therapies will succeed:

What are the particular challenges….

the *specificity* of RM as a field:

Challenges relating to any emergent field	Is there a specific challenge for RM?
Clinical trials • Complex environment overseen by multiple bodies • Inappropriate existing infrastructure (eg Trial costing templates).	**Yes.** There are particular safety and efficacy challenges deriving from the perceived complexity and fragility of live material - inherent variability and complexity of working material makes definition of *critical quality attributes* more difficult
Regulation: • Burden of the many relevant legal provisions • Heterogeneity in implementation of provisions • Major difficulties associated with classification of products	**Yes.** Classification of therapies poses specific challenges to developers and regulators.
Manufacturing/scale-up: • Underdeveloped infrastructure for scale-up & transport to the clinic • Lack of consensus regarding quality assurance • Lack of suitable QPs at clinical sites	**Yes.** Although scale-up, quality assurance and related issues are seen in many novel applications, they are particularly difficult for RM products which are based on living tissues and cells

Implications for regenerative medicines

- Live tissues/cells require specialist **infrastructure & skills for transportation** and preparation at the clinic (including Clinical Apheresis Unit)
- New manufacturing & logistics arrangements re procuring/handling live tissue
- Onsite manufacturing will require **expensive bioprocessing equipment** such as cell separation & expansion systems, systems for transfection etc.
- Hospitals may need to act as procurement service for a third party. **Contract arrangements for this can be complex**. How might QA and liabilities be distributed among parties?
- Some proposed **risk-sharing commissioning schemes need coordinated data-collection** infrastructures.
- Regulatory/quality requirements – relating to Pharmacy processes and JACIE accreditation

The delivery of regenerative medicines will require significant organisational/institutional adjustments

Webster A and J Gardner (2019) Aligning technology and institutional readiness: the adoption of innovation, *Technology Analysis and Strategic Management*, DOI: 10.1080/09537325.2019.1601694

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Routledge
Taylor & Francis Group

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Aligning technology and institutional readiness: the adoption of innovation

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ABSTRACT

This paper explores and develops the concept of 'readiness' as it relates to the adoption of innovation. In particular, the paper discusses readiness in regard to the notion of 'technology readiness' levels, widely used today by both producers and users to monitor and manage emergent innovation. The paper argues that, while useful, this notion needs to be informed by and subsumed within a broader concept of 'institutional readiness'. The latter is especially important in conceptualising how new technologies are actually adopted in organisational settings. The paper develops a model of institutional readiness that recognises the saliency of technology readiness but which embeds it within a broader socio-technical framework. This is illustrated with reference to the emerging field of regenerative medicine.

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Technology readiness; innovation; adoption

Gardner J, Webster A and J Barry (2018) Anticipating the clinical adoption of regenerative medicine: building institutional readiness in the UK, *Regenerative Medicine*, Jan 2018.

2. What might this look like – what organisational demands will need to be met?

Developing the concept of ‘institutional readiness’

- Formal categories
- Contrast with TRLs
- Criteria for assessing IR at a clinical site

IR Category	Operationally defined *for any sector*
Demand for new technology	Institution has key actors engaging with and identifying new technologies that meet field/organisational needs
Strategic focus	Institution has identified potential new technologies and determined their relation to existing ones.
Relative need and benefit of new technology	Institution has key actors assessing capacity to take-on and develop new technologies within current and future contexts
(E)valuation processes in place	Assessments of the (diverse) values of new technologies are undertaken and shared
IR enacted through specific enablers within and outside of the organisation	Key individuals/groups are formally tasked to enable adoption especially in regards to meeting standards and regulatory requirements
Receptivity	Novel institutional structures are created, in anticipation of expected challenges/affordances presented by new technology. These structures reflect the need to retrain staff, the construction of new innovation spaces and new technology platforms etc
Adoptive capacity	Novel technology aligns with institutional priorities and organisational capacities. Initial problems and unanticipated challenges/affordances are identified and seen to be manageable.
Sustainability	Novel technology is routinely produced/used/assessed within institution. Current institutional arrangements and resources are sufficient for routine and ongoing production, assessment and deployment.

Adoption of emerging therapies: comparing Technology Readiness Levels and Institutional readiness

Challenge of adoption have been overlooked e.g linear notion of innovation - Technology Readiness Levels (TRLs)

Main concerns re TRLs relate to:

- the need to recognise the growing complexity of a system as 'levels' actually combine and the discrete components become more porous at their interfaces
- the difficulties associated with failure to integrate the TRL process within an organisation's business model and processes
- the lack of precision in assessing TRLs and the 'tests' used to do so such that validation measures are open to doubt.

Given the above a 'mature' technology as defined solely in TRL terms may itself not be 'ready' for use in certain systemic (organisational) conditions

Contrasting IR with Technology Readiness concepts

	Technology readiness	Institutional readiness
Relation between categories	Sequential hierarchy of *'levels'*	Discrete *capacities*
Criterion	Risk reduction	Organisational functionality
Adoption via	Assessment of maturity of technology	Normalisation within institutional practices
Material aspect of technology/product	Stable and standardised	Co-produced and localised
Implementation	Incorporation of *working* technology	Learning by trying – a *workable* technology

3. The Advanced Therapy Treatment Centres

IR Category	Operationally defined in an ATTC at the organisational level
Demand for new technology	Prevalence of target indication and capacity to treat expected patient cohort
Strategic focus of ATTC	Ensure opportunities for staff training and skills in logistical coordination Appropriate infrastructure for administering treatments Tie-in with the Cell and Gene Therapy Catapult
Relative need and benefit of new technology	Appropriately trained Qualified Persons (role of Pharmacy) and appropriate quality assurance staff and systems to determine benefit
(E)valuation processes in place	Assessments of the RM therapies are undertaken and shared Agreement among stakeholders on what constitutes evidence of success/cost effectiveness of RM therapies.
IR enacted through specific enablers within and outside the ATTC organisation	Alignment of new therapy with clinicians, administrators, managers and external regulators; Aligning/modifying work practices across these groups (eg Trials Unit)
Receptivity of the ATTC	Novel institutional structures are created: Access to GMP-licensed facility (and associated GMP expertise) Access to and capacity for appropriate bioprocessing systems Capacity and resource of data-collection infrastructures for monitoring outcomes for products classified via an Adaptive (regulatory) Pathway – key for reimbursement based on outcomes rather than initial discounts
Adoptive capacity of the ATTC	Novel technology aligns with institutional priorities : ATTC consortium embedded in wider hospital delivery system – (eg the ATTC's 'Community of Practice') Opportunities for meaningful patient involvement
Sustainability	Novel technology is routinely produced/used/assessed within institution. Clinical skills for preparing patients and administering treatments within regional and national clinical trials networks

Key implications for NAATTC partners

1. New funding for Advanced Therapy Treatment Centres – 2018-22:
- Act as an effective pilot – 'implementation laboratories' – means there is a need to decide what outcomes can be expected
- How to build on existing system (eg NHSBT) learn from other areas and build new data systems

2. Need to *align* 'technological readiness' with 'institutional readiness' – from *working* to *workable* innovation

3. The IR 'template' now being rolled out– priorities, existing and new resources needed, division of labour

For example – part of the draft template…

Criteria relating to the RM technology or technique	Criteria relating to the potential site of clinical delivery
Target indication for the ATMP	Existing expertise in disease area?
	Capacity to treat expected patient cohort?
	Opportunities for patient / public involvement & collaboration?
Complexity of intervention	Logistical coordination - Planning, procurement, production and distribution (within shelf life) for each individual patient?
	Appropriate infrastructure for administering treatments?

4. Conclusion

i) Acknowledge specific challenges of RM in clinical context

ii) Need to understand how TRLs and IR criteria can be made to work together: levels of readiness are given meaning only where there are forms of institutional readiness that ‘bring them to life’ and make them workable.

iv) Key role then for specialist clinical centres such as the NAATTC.

Further information at:

https://www.eurostemcell.org/regenerative-medicine-special-report