Towards a standardised and personalised in-vitro tool for 'functional' testing of 3D-printed (non)degradable orthopaedic implants

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For some time, researchers and companies are developing means to better mimic the 3D human tissue environment to make the implant development process more reliable, thereby (a) reducing in-vivo trial associated complications, (b) lowering costs resulting from late-stage failures, (c) ensuring quick abandonment of dead-ends, and (d) shortening the development process so that life changing implants reach the market sooner.
Development of 3D assays at the meso-scale have remained a challenge however, as the degree of precision required to emulate in-vivo cell-to-cell communication has proven elusive. Nowadays bioreactors enable a first step towards the in-vitro creation of more relevant cell and tissue-like environments for standardised and functional implant screening.
Currently, the ISO 10993-5:2009 guidelines describe the standard for biological in-vitro evaluation of novel materials for medical use. Non-toxic behaviour is indeed an essential material prerequisite for novel medical, implantable, applications. It, however, provides limited information on the actual device functionality. With the increasing number of geometrically more complex, customised and biologically active devices, also as part of the precision medicine revolution, including personalised and regenerative therapies, more functional in-vitro assays are needed.
Hence, there is a need to optimise decision making early on in the implant development process, supported by the growing insight that the relevance of preclinical models towards final patient outcome is limited. Establishing predictive correlations between implant bulk and surface properties and functional behaviour related to patient outcome will be essential to secure a sustainable clinical implementation of these personalised implants.
The development of a novel in-vitro standard can support the shift from assessing bio-tolerability and -compatibility towards bio-functionality. Using customised, closed, automated, stand-alone bioreactors, standardised functional screening of novel implants can become possible. Not only will these systems support the development of reproducible, operator-independent methodologies, they also enable testing of clinically relevant implant dimensions, geometries and other physicochemical surface and bulk features. Such systems also allow 'running' more complex, physiologically relevant and more patient-specific biological models on a lab scale.
The development of bioreactor-based standards for in-vitro 'functionality' testing of open porous, additive manufactured (non)degradable orthopaedic implants, using QbD-based 'functional' assessment of cell-medical device interaction in combination with in-silico predictive tools, will assist clinical translation of this next generation, customised and biologically active implants. Establishing R&D capacity for in-vitro screening of cell-medical device interaction at this meso-scale, coupled to multi-parametric data assessment and processing will enable improved decision making early in (personalised) medical device development.

A part of the research for this paper was financially supported by the Prosperos project, funded by the Interreg VA Flanders – The Netherlands program, CCI grant no. 2014TC16RFCB046.