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Harnessing the Global Brain in Medical Imaging: 3DnetMedical, Network-Centric Innovation in the Cloud – Our experience.

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Abstract: *Medical Imaging is a technology-driven field that spans across many medical specialties. The surge to provide physicists with sight – and insight – about the human anatomy, physiology, and diseases is a powerful stimulant for continuous innovation through multidisciplinary collaboration. Challenges, ideas and talents are all over the place. Unfortunately, market reality shows that innovation is still largely dictated by OEMs, and the alternative "open" pathways mostly remain confined inside the clusters in which they have been created. The IT revolution in healthcare has given opportunities for new approaches. In particular, by using Cloud Technology to build a network-centric ecosystem, Biotronics3D is aiming to shift innovation in Diagnostic Imaging from "business-centric" to "creative problem-solving" solutions, designed by and for the community.*

1. Shifting Innovation Paradigms in Medical Imaging

Medical imaging, which encompasses activities such as measurement, reconstruction, analysis and representation of biological structure and process as images, is one of the fastest growing areas within medicine at present, both in the clinical settings and in research and development. The tremendous advances in hardware technology have enabled imaging modalities to acquire a vast quantity of anatomical and functional data in reduced time, providing clinicians and scientists indispensable information for the understanding, modelling, diagnosis and treatment of diseases. This explosion also means that visualisation and analysis software has become an integral part of the diagnostic machines to handle and process such large sets of complex and detailed images in a simple and efficient way. To date, fusion of technologies, computer aided detection (CAD) and automated image analysis applications are the major drivers of the medical image analysis market.

Although the market has seen a boost since the IT revolution in healthcare, global medical device original equipment manufacturers (OEMs) such as Philips, Siemens and General Electric largely dominate the medical imaging space. Many smaller players are making efforts to make their mark by bringing innovative solutions to the market, but the major revenues remain generated through supplying services and programs to the OEMs. This strategy among large corporate players to leverage licensing agreements, establish partnerships and work collaboratively with technology suppliers has been growing over the last decade while strategic acquisitions have gone down.

From Close to Open Innovation

Over the last few years, open-source software (OSS) development for medical imaging has grown significantly. Open-source programs are usually developed as a public collaboration and made available for use, modification, enhancement, and redistribution, enabling individuals and groups to produce high-quality tools geared to meet specific user needs.

The current burgeoning of independent OSS tailored medical analysis applications and open platform solutions, such as XNAT and CommonToolKit (CTK), which focus more on holistic approaches to support medical image computing community development and allow users to rapidly add new processing and analysis tools as plug-ins or extensions, clearly demonstrate a desire to create innovative solutions through sharing and cooperation in the development of medical software applications. The fact, alas, is that the majority of these OSS solutions, which haven't been taken by a commercial entity, remain confined in the clustered environment in which and for what they have been created, suggesting that that OSS alone cannot guarantee success.

However, the example set by OsiriX (a Mac OS-based OSS) as a generic imaging platform that can be adapted to a variety of applications while providing the basic tools for multi-dimensional imaging and image processing, shows how open software development for medical imaging tools can be successfully designed, implemented and disseminated [1]. OsiriX owes its marginal success to its design, done by radiologists for radiologists, and the robustness of its code, which makes it a very stable product for use in clinical and research applications. Its sustainability resides in its partnership with commercial vendors and in the creation of OsiriX Foundation, which promotes and awards the development of image processing and analysis plugins for OsiriX.

2. 3DnetMedical CLOUD platform: Our Approach.

2.1 3DnetMedical: A Cloud-based Platform for Innovation

3DnetMedical is a cloud environment and can be accessed via web-browsers with a zero-footprint client, from anywhere, and at any time. Thus, the access is operating system-independent and installation free and collaboration requires no hardware or software setup. The following is an overview of the system, a more detailed and technical description is available in [2].

2.1.1 On-demand solution

3DnetMedical is a complete on-demand solution (public and/or private cloud) that provides a fully secured data management system to leverages healthcare organisations' IT hurdles in a cost-effective way, including multi-point access, transfer, migration, storage of imaging data and associated information, worklist management and interaction with hospital/clinic IT systems (RIS/PACS) or/and imaging modalities directly through standard protocols (DICOM & HL7). It also offers powerful advanced visualisation, customised or protocol-driven workflows, pipeline processing capabilities, as well as reporting tools accessible from any device connected to internet.

2.1.2 Collaboration

As diagnostic imaging is extending across an increasing number of medical specialties and interdisciplinary partnership is becoming the cornerstone of contemporary scientific research, a particular focus has been put on simplifying data-sharing processes across organisations and collaborations between peers, where ever they are in the world.

2.1.3 Platform for Innovation & Commercialisation

3DnetMedical provides the development environment, tools and support for independent developers, academic institutions and R&D organisations to implement or integrate their *Intellectual Properties* into 3Dnet cloud system. Developers have the opportunity to implement analysis modules directly in 3Dnet infrastructure via the development kit, which comes with a library of common components and functions to increase the speed of module development, or seamlessly integrate their externally developed code with the minimum of effort via 3Dnet wrapper mechanism.

Through 3Dnetmedical marketplace and the existing customer base, innovators can then promote their outcome and create commercialisation opportunities (retaining their IPs), obtain the seed customers and gather early product feedback that will lead to informed innovation iterations.

2.2 Network-Centric Innovation

Network-Centric Innovation is defined as “an externally-focused approach to innovation that relies on harnessing the power of networks and communities to amplify innovation reach, accelerate innovation speed, and improve the quality of innovation outcomes” [3], and is built around *creation spaces* where communities can address innovation opportunities and challenges, generate and share ideas and insights, and shape them into strong concepts that in turn create new value.

These networks, funded by private or public institutions, are well established in Medical Imaging, and can be found in both research, scientific or clinical, (for the development of diagnosis tools, treatment efficacy, etc.) and clinic (improvements on delivery of care). Unfortunately, they often exist and operate in separate worlds. Therefore the challenge lies in providing the appropriate contexts for these networks to come together and engage in collaborative experimentation, tinkering, and innovation.

3. Network-Centric Innovation Models in Use

3.1 Picking & promoting the right ideas from the “Creative Bazaar”

The Institute of Cancer Research (ICR) is one of the world’s most influential cancer research institutes, and forms with The Royal Marsden Hospital the largest comprehensive cancer centre in Europe. Over the last 10 years, the ICR Scientific Strategy has been focusing around the three interlinked themes of genetics and epidemiology, molecular pathology, and therapeutics. The ICR has an outstanding record of achievement in understanding the genetic basis of cancer, as well as in drug discovery and development.

Research in clinical imaging is also playing an increasingly preponderant role in ICR's global scope of "developing a personalised cancer medicine", to better detect, evaluate and plan the treatment of cancer, and better assess the action of cancer therapies. This encompasses non invasive approaches to assess various facets of tumour biology and definition of imaging biomarkers that reflect physiological and metabolic properties.

3.1.1 Dynamic Contrast Enhanced MRI (DCE-MRI) Analysis Module

The ICR have been a significant contributor in the development of pharmacokinetic models for DCE-MRI in tumour assessment. In 2006, the ICR produced a full research-driven application in IDL called MRIw [4], available on demand. The overall complexity of the methodology, difficult interpretation of the output parameters and cumbersomeness of the application, have, unfortunately, confined the method to a niche group of clinical researchers only.

The collaboration between ICR and Biotronics3D saw MRIw fully re-implemented into 3Dnet platform by a developer at Biotronics3D, under the guidance of ICR's engineers and clinicians, to a commercial software standard. Data management and multi-dimensional reviewing were inherent to 3Dnet, data processing speed was largely improved enabling full tumour analysis instead of a slice-by-slice approach, and the overall look, feel and usability provided a smoother experience. Integrating DCE-MRI analysis into a clinical workflow contributed to a greater appeal and interest from a larger range of – yet – clinical researchers in the community. Alongside the distribution of the module itself, Biotronics3D has also been providing support to users through guidelines and recommendations harvested from ICR, as well as live demo and trainings.

Short before the Radiology Society of North America (RSNA) conference end of November 2012, the Quantitative Imaging Biomarkers Alliance released a comprehensive guideline on the advantages and usage of DCE-MRI Quantification [5]. This guideline is intended to stimulate the medical practitioner community to better understand and use DCE-MRI. Should this succeed and a new module would be derived from the original 3Dnet-MRIw; simpler and more clinical routine workflow-driven.

Pulling and integrating ICR's IP at relatively "early" stage could have been perceived as a risky choice. However, distributing the solution only to researchers inside 3Dnet Community and maintaining a continuous interaction and communication – between the them, Biotronics3D developers and ICR experts – not only allowed them to better grasp an understanding of the concepts and gain confidence on the methods, but also identify the key components useful for clinical diagnosis and disseminate their own practice.

3.1.2 MRI Breast Analysis Module

From August 1997, the ICR coordinated a five year multi-centre trial for Magnetic Resonance Imaging for Breast Screening (MaRIBS). The findings indicated that Contrast Enhanced MRI was more sensitive than mammography for cancer detection [6]. Throughout the trial, the ICR implemented and validated series of tools including proprietary uptake and density maps, as well as automated morphological lesion segmentation and classification of time intensity curves (TIC), which were used to analyse the datasets.

In the last couple of years, the various publications comparing MRI breast screening with mammography and ultrasound only confirmed that “breast MRI is a valuable imaging tool in addition to mammography and ultrasound, which allows the identification of otherwise occult breast disease. It is particularly useful in the evaluation of patients with breast cancer and for screening women at high risk of breast cancer” [7]. However, for these patients with breast cancer, MRI truly has a core advantage as the combined analysis of morphological and dynamic images, especially using CAD, allows discrimination between benign and malignant lesions [9].

Today, CAD has become a must-have feature for MRI breast analysis as a workflow tool. MRI breast CAD helps radiologists manage the large sets of data, it calculates critical measurements, corrects for motion artefacts, and characterizes abnormalities on the images. These automated steps save the radiologists’ time, enhancing their overall performance.

This context represented an obvious opportunity for ICR to package its existing tools into a solution that is highly demanded by 3DnetMedical users, and at the same time to introduce its new – yet already proven – measurements. The ICR-Biotronics3D collaboration for the breast analysis module was a one-year funding project and involved a developer on ICR side to re-implement, update and optimise the existing tools in 3Dnet environment, supported by a developer at Biotronics3D, who was also designing the UI and implementing all the client/server communications.

At the point of writing, the project is now complete in terms of IP transfer, and is entering the stage of engaging seed users inside 3Dnet Community to get initial requirements for a minimum viable product, as well as feedbacks on functionalities, as initial step of an iterative innovation process. Alongside, another set of “advanced” users’ needs to be identified to test and endorse the benefits of the new measurements as improving diagnostic process; meaning channelling further efforts for the learning and appropriation of a new knowledge at the users’ end.

3.2 Orchestrating Innovation

VIGOR++ is an international research project that aims to create a personalised gastrointestinal tract model, which facilitates accurate detection and grading of Crohn’s disease, so that the management of the disease becomes personalized, patient friendly, and effective. VIGOR++ is supported by the 7th Framework Programme of the European Commission in the context of research towards the Virtual Physiological Human.

The proposed technology builds on multi-scale information from patients, including laboratory, MRI, colonoscopy and microscopy (histopathology) data. A novel integration of existing models is employed to predict features on the molecular to cellular scale (microscopy/colonoscopy) from descriptive properties at the organ to patient scales (MRI/laboratory). The benefits are early diagnosis, improved therapy planning and a better quality of life for patient.

The techniques are integrated in the 3DNetMedical.com medical imaging cloud service, to make them immediately available in a clinically usable environment. Notably, tools could be rapidly commercialised and delivered as an optional toolbox to clinical sites.

The consortium includes various academic, clinical and industrial partners with different roles:

- University College London Hospitals is in charge of data acquisition and management, pushing images and associated information in 3Dnet cloud and assuring their compliance/anonymisation/access rights.
- Clinicians and clinical researchers from the Academic Medical Centre, University of Amsterdam (AMC) have two important clinical roles. **(i)** They analyse the uploaded data, annotating and labelling regions at risk in 3DnetMedical directly – no need to download the data and open third party application – then only need to save their work. **(ii)** They validate the processing methods described in the next point and analyse the derived information to extract relevant statistics and identify potential biomarkers of Crohn's disease.
- The members in Zuse Institute Berlin, the Swiss Federal Institute of Technology Zurich and Delft Institute of Technology can access the clinical expert information any time and use it in the implementation of their various processing modules. These modules include registration, segmentation and quantitative analysis tools, written in C++ and Matlab, and directly integrated into 3DnetMedical. All outputs of the processing modules are automatically inserted back in the studies and made available to AMC for validation and further analysis.
- Biotronics3D acts as technical leader to integrate and support all development parts, including specific data management, custom visualisation, and modules integration.
- Vodera Ltd. oversees the value of the project, coordinates the dissemination and exploitation of the product, and assesses potential future applications, inside and outside 3DnetMedical ecosystem.

Over the course of this on-going project, (1) the datasets and associated information files are uploaded once, and then accessed only within the secure environment of the cloud; (2) the various analysis modules operate independently during development, but should be integrated in an automated pipeline at the final stages.

Implementing such project inside a unified environment should undoubtedly "ease" and speed up the whole process of value creation, but should also facilitate the synthesis and dissemination of knowledge and know-how, which is where, for the purpose of patient care, the real value of innovation truly lies.

4. Conclusion: What are we learning along the way?

Innovation in healthcare has this particularity that its finality is health improvement and patient care. Any discovery that provides better understanding of pathology, any idea that offers new opportunities for more efficient diagnosis and treatment, ultimately needs to reach the very person at the point of care who will deliver a diagnosis.

For this very reason, innovation in healthcare cannot and should not be solely defined as the development of new customer value through solutions that meet new needs, inarticulate needs, or old customer and market needs in value adding new ways. Innovation in healthcare encompasses a very strong knowledge value that needs to be transferred along with the solutions. However, unlike information, knowledge tends to reside in individuals. Knowledge sharing requires trust-based relationships and a sharing of practice.

Building these relationships does not depend only on providing the technology to enable communication between the parties. As a company, we need to become coordinators and active participant in the networks, supporting, channelling and mobilizing the independent entities in the pursuit of distributed, collaborative, and cumulative innovation. We need to build a space, an ecosystem, in which users, innovators and entrepreneurs can interact, collaborate and benefit from each-other, all participating and becoming co-creators of innovation by sharing their expertise and experiences.

- *Users*, the clinicians and researchers, who face challenges on a daily basis for diagnosis and data analysis, could benefit from external experts' inputs who can suggest or offer creative approaches to addressing their challenges. Given the opportunity to express their needs, or simply share their experience, they can also inspire innovators and entrepreneurs, who may come from completely different fields, for new ideas or paradigms.
- *Innovators*, the scientists, research groups or academic institutions, would implement applications better and faster through facilitated interactions with clinicians, who could provide data and expertise to validate their processes and methods.
- *Enterprises*, independent software vendors, innovation management services providers and innovation capitalists, would gain a better understanding of the value of an innovation and see a reduced risk, even in the preliminary development phases, if a dynamic is already established between innovators and users. They could even help develop and refine the ideas to a stage where their market potential is validated.

Furthermore, it appears clear that a constant focus on building long-term relationships with participants and creating opportunities for repeated interactions is crucial to maintain continuous innovation, not just a succession of episodic and marginal short success stories.

Finally, the growth and sustainability of our ecosystem relies on our capability to constantly stimulate and manage the flow of knowledge, not on owning it.

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