Integrative Cancer Research
INTEGRATE
Through Innovative Biomedical Infrastructures

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inside

editorial

All INTEGRATE partners and I are excited to share with you, in this second issue of the INTEGRATE Newsletter, the progress made in the last six months, the results materialized in the first INTEGRATE prototypes, and our plans for the future.

This time, the INTEGRATE partners FORTH and Custodix led the production of the newsletter, highlighting their contribution to the project. We hope this will help you get to know these partners and their activities within INTEGRATE better!

The "Focus" article on pages 2-4 introduces the first two INTEGRATE prototypes developed. The first is a Patient Eligibility Screening application based on the molecular screening scenario, which enables physicians to check if a patient is eligible for a selected trial. The second is the INTEGRATE Analysis Platform - which is a web-based framework that facilitates the statistical analysis of clinical and molecular data.

On pages 5-6, p-medicine, another exciting project in the eHealth area, is presented. The INTEGRATE Consortium partners have set up a close collaboration with p-medicine aiming to exchange experiences, jointly address common challenges and share relevant solutions and tools.

The "Viewpoint" section features on pages 8-9 an interview with Nikolaus Forgó, Professor of Legal Informatics and IT-Law and Co-director of the Institute for Legal Informatics at the University of Hannover, Germany. Prof Forgó has extensive experience in all fields related to ICT law, in particular on data protection and data security law, and ethical and legal issues in eHealth. He answers questions about important data protection issues in the context of INTEGRATE and shares his views on the best approaches to data sharing in cancer research in general, in order to ensure full and future-proof compliance with legal and ethical requirements. Due to his extensive expertise and the relevance of the topics addressed, Prof. Forgó's recommendations are highly applicable even beyond the context of INTEGRATE.

Finally, the "Life in INTEGRATE" and "Events" sections inform you of the latest developments and upcoming activities of the INTEGRATE Consortium.

The INTEGRATE Newsletter can be received by sending a request to big@bordet.be and is also posted on the INTEGRATE website www.fp7-integrate.eu, which I warmly invite you to visit for updates.

Anca Bucur
INTEGRATE Project Coordinator

The INTEGRATE prototypes

By Brecht Claerhout and Kostas Marias

One of the major deliverables of the INTEGRATE project is the platform itself (software implementation). In the first year, the project has successfully delivered two prototypes – shown at the annual review of the project organized by the European Commission – each tackling a subset of the functionality of the overall envisioned platform.
The first prototype is a patient screening application that enables physicians to check if a patient is eligible for a selected trial. The second is the initial iteration of the INTEGRATE Analysis Platform, which is a web-based framework that facilitates statistical analysis of clinical and molecular data.
Both prototypes integrate the full INTEGRATE software stack – albeit with reduced functionality – which makes them all the more interesting as proof of concept of the project's approach.

Moving towards computer aided patient recruitment

The patient screening prototype fits within the wider setting of how the Breast International Group (BIG) expects to screen patients for many of its trials in the future.

When physicians participating in a BIG clinical trial believe that one of their patients may be eligible, they need to formally verify whether the patient meets all of the trial's eligibility criteria. For this, physicians must acquire all necessary clinical information and check that the criteria are fulfilled. For an increasing number of trials (e.g. those involving drugs that target specific oncogenic molecular aberrations present in sub-groups of patients), checking eligibility is a multistage process that also involves the molecular testing of tumour tissue.

Identifying patients who meet all the criteria of a given trial is today still a largely manual process. It fully relies on physicians being aware of which clinical trials are open to patient recruitment and having a fairly detailed idea of the respective eligibility criteria of each one.

One of the objectives of INTEGRATE is to facilitate the patient recruitment process by maintaining a trial registry for BIG (containing all open protocols and trial eligibility criteria) and providing computer assistance for streamlining the eligibility criteria testing (i.e. automating, the criteria testing).

The patient screening application being built into INTEGRATE will provide automated checking of eligibility criteria based on structured patient data present in electronic health records (EHRs) and clinical trial data management systems.

When a physician wants to screen a patient for eligibility, he or she will start the tool, select that patient and choose the active BIG trials for which the patient should be screened (Figure 1).

Consequently, the tool will run the screening service for each of the selected trials. The output of the automated matching (automated eligibility evaluation) is an indication of the number of criteria that the patient either meets or does not, as well as those criteria that cannot be automatically evaluated. The latter can occur when criteria are too complex to be automatically evaluated, when there are insufficient data or when criteria are simply not computable.

The tool will then allow the physician the possibility to delve into further detail for each of the available trials through an attractive and intuitive user interface. The canvas style workbench (Figure 2) will give the physician an overview of the individual criteria of a trial and the eligibility of the patient. In this workbench, the automated eligibility evaluation can be manually verified (the data on which the automated evaluation is based can be displayed) and, if necessary, overridden. Similarly, the tool will allow automatically calculated eligibility outcomes to be marked as "validated" by a physician.

This software has the potential to significantly simplify the patient screening process, by removing the tedious work (e.g., making sure that all trials are taken into account) while still leaving the physician fully in control of the final decision.

Data sources for screening

The screening service will be capable of taking into account different data sources for evaluating the criteria.

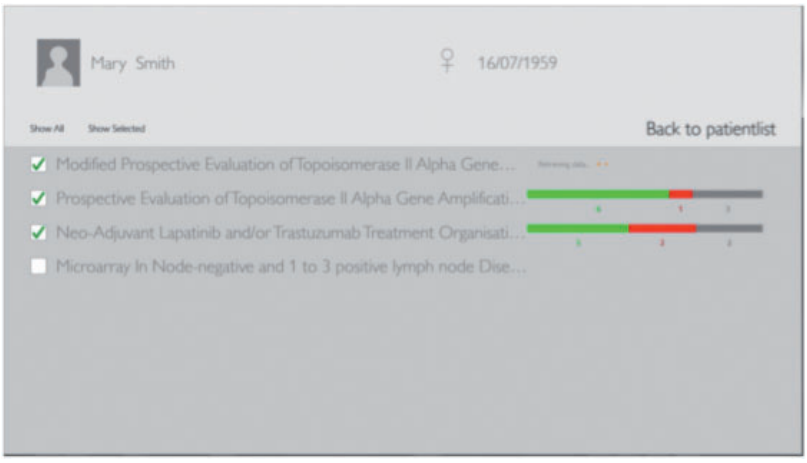

Figure 1: Screen where a physician can select which trials the patient should be screened for. One can see that the screening for the first selected trial is still running.

The most obvious source of relevant patient data is the local EHR in the centre where the patient is treated. Local EHRs are "INTEGRATE-enabled" by creating an export into a local INTEGRATE compliant Clinical Data Warehouse (CDW). The INTEGRATE security infrastructure will ensure that physicians can only perform screening on their own patients and can only use EHR data from their own centre.

In the context of the trials run under BIG, in addition to the local CDWs (EHR extracts), the screening application will also check a shared platform CDW. This CDW collects data that is rather specific to the trial screening itself and would typically not appear in the EHR. Examples include the results from the molecular screening of a tumour for the purpose of checking trial eligibility (this could eventually be sent to the platform by an external lab) or specific data that is entered manually by the investigators to enable automated screening. Obviously this centrally-stored data is also protected by the security framework, which allows physicians access only to data from their own patients.

Figure 2: View on the canvas where a physician can check the different eligibility criteria. On the left is a docking bar for temporarily "parking" widgets. The canvas contains the widgets associated with each of the criteria. In this screen-shot, the user has selected the GPT<1.5N criterion, making this widget "active". When a widget becomes active, the menu for overriding or validating the automatic evaluation unfolds (middle of picture).

Next steps

The screening application prototype built during the first year of INTEGRATE fits within the wider challenge of improving processes related to clinical trials. The number of clinical trials run each year is decreasing (especially in Europe), with obvious consequences for research and ultimately on care. This is partly due to the increasing difficulty to recruit patients for the targeted drug clinical trials, which have more complex eligibility criteria. Automating the evaluation of eligibility criteria is seen as one possible solution to increase the efficiency of the recruitment process, both in terms of cost and quality.

The presented prototype is still in an early stage, there is plenty of room for improvement that can be tackled during the remaining period of the INTEGRATE project. One example of an additional functionality could be the possibility to rank the trials for which a patient could be eligible according to customisable rules. In case a patient is eligible for multiple trials, the system could then determine the better enrolment choice, according to local practice (a ranking rule). This ranking rule could for instance point the physician to a trial whose accrual rate is slower than expected (e.g. because of restrictive criteria). Of course, a lot of different ranking rules could be implemented. It should however be stressed that in any case, the decision remains at the discretion of the physician (fitting the overall philosophy of "computer aided" tools).

As the acceptance of a tool is largely determined by its usability, the screening prototype includes an innovative user interface, which is designed to feel natural to the users. The application has a very simple flow (select the patient, then select the trials to screen, then look into the criteria detail) and the user interface aims to provide an intuitive way (mimicking physical actions) of working with "information" (cf. modern tablet computer interfaces). In the upcoming months several tests will be performed with user-groups (from the BIG consortium and from partner EU projects) to collect feedback on how the usability could be further improved.

Finally, this early working demonstrator will be the ideal tool to inspire all stakeholders and encourage them to think about the future of this prototype.

Analytical tools for data sharing

The main objective of INTEGRATE is to provide users with web-based access to a collaborative, multi-functional and easy-to-use environment for exploiting, analyzing and assessing the quality of large multi-level data. The aim is to provide physicians and other researchers with a set of web-based tools with which to easily analyse clinico-genomic data in order to get – for selected cohorts of patients – simple statistics on selected parameters, perform survival analyses, compare regimens, and obtain genomic analysis results. INTEGRATE is being built in a way that will not require users to have any prior expertise in using such tools, or any software or libraries installed on their computers.

Because the available data are so heterogeneous – ranging from clinical and genomic to imaging information – the INTEGRATE architecture is non-monolithic. In other words, each component of INTEGRATE is responsible for implementing a specific task.

A core tool – and the second prototype developed to date – is a semi-automated software platform for statistical analyses, called the INTEGRATE Analysis Platform. This is to be used together with Central Pathology Review and Predictive Modelling tools, still in development.

To enhance the platform's functionality, the analytical tools will be coupled with an intuitive clinical data browser that takes as input query results and filters data according to any of the available parameters (i.e., clinical or genomic) through a user-friendly interface. Subsequently, the user can select specific columns over the filtered cohort of patients and run tools by just pressing a button. The results of the analysis including the filtered patient cohort are presented in a dynamic report that can be stored and used for future reference

The need to store and reuse data means that an essential part of INTEGRATE will be a centralized data warehouse, involving data security, flexible data access control, semantic operability and data querying, also in development. The current version of the INTEGRATE Analysis Platform queries directly on the database of the platform and then filters the results using AJAX in order to provide instant updates of the user interface, thus providing a feeling of a «native application» to the end user. In the next release of the Analysis Platform the functionality to add and configure connections to the external central data-warehouse of INTEGRATE will be implemented, where the data source will be either a database engine or a web service.

The INTEGRATE Analysis Platform

The statistical prototype – the INTEGRATE Analysis Platform – is a semi-automated software platform for the analysis of the heterogeneous data, using descriptive statistics and incorporating bioinformatic tools for:

- Rapidly assessing the variability, dependency and the distribution of certain clinical characteristics across patient populations;
- Making comparison tests and evaluating response rates to different treatment regimens when applied to a certain patient population;
- Defining whether specific clinical parameters are surrogate markers for patient survival, involving the modelling of time to event data in survival analysis;
- Estimating the degree of association between biomarkers, extracted from pathology or radiology imaging data, and the clinical response of a patient group;
- Performing quality control tests to the genomic data, identifying statistically significant genomic information that discriminates subpopulations (i.e., patients who have achieved pathological complete response vs. those who did not), and applying unsupervised learning techniques to the entire genomic information.

The prototype then assists users in evaluating the results of the statistical analysis by creating dynamic reports that can be updated automatically if the data or the analysis changes. These reports are generated in PDF format, giving a full description

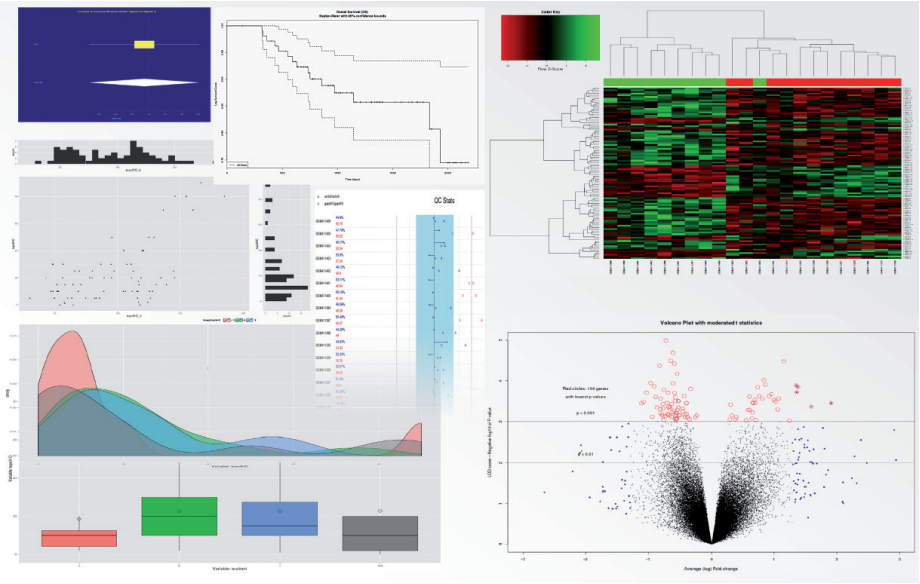

Figure 3: Indicative analysis results that the clinician easily obtain from the platform

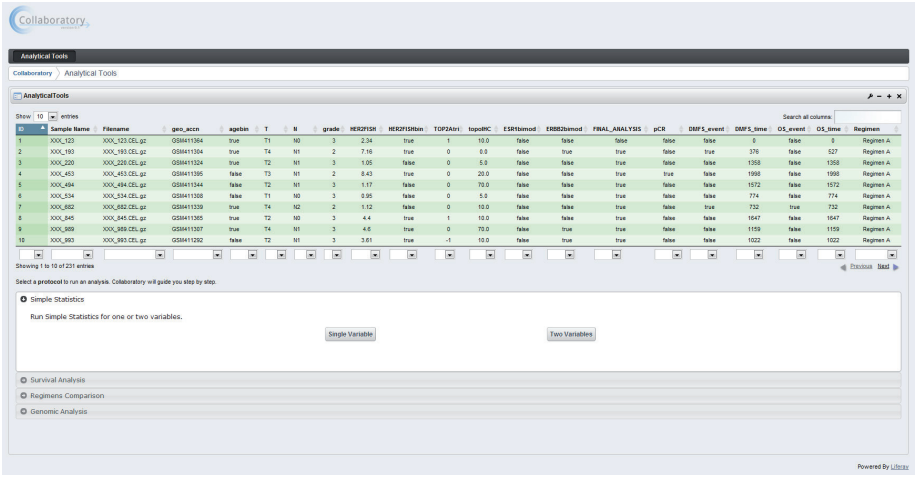

Figure 4: The Analytical Tools as a part of the INTEGRATE Analysis Platform

of the research question addressed, the applied tool, and the statistical results.

The architecture

INTEGRATE is being constructed to provide users with a web-based interface that supports user authentication, data handling, execution of the statistical tools, and visualization and storage of the analysis reports. To achieve this goal, the programming of the different environments and languages adopted to implement the platform's facilities, and the connectivity process that allows the interaction between these components, have been kept at the back-end of the platform, hiding the complexities of the computational infrastructure.

From a technical perspective, INTEGRATE's Analysis Platform is based on the Liferay Portal[1], which itself is an enterprise web platform using Java technologies. We decided to choose this third party open source portal mechanism because Liferay is supported by a devoted group of developers who have adopted a cycle of frequent updates, whereby security enhancements, optimizations and new web technologies are provided in each cycle. Another reason is that by upgrading and extending the functionalities of the CMS we will be able to provide a consistent user interface for all the modules of INTEGRATE, ensuring a seamless user experience.

R language was used to implement the statistical tools[2]. R provides a powerful suite of tools for statistical analysis, a highly extensible coherent system for software development, and good connectivity with other software environments. To facilitate embedding R functionality in our java-based interface, a client/server concept using TCP/IP protocol[3] has been used to communicate between the R system and the end-user, enabling interaction between the platform and the execution framework. At the

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p-medicine: from data sharing and integration via VPH models to personalized medicine

By Prof. Dr. Norbert Graf, Project Coordinator of p-medicine, on behalf of the p-medicine Consortium

Progress in medicine is currently transforming the nature of healthcare from reactive to preventive. The changes are being catalyzed by a new systems approach to disease that has triggered the emergence of personalized medicine - a medicine that focuses on the integrated diagnosis, treatment and prevention of disease in individual patients. Additionally, patients themselves contribute to this transformation by obtaining ever more information from the internet and realizing that personalized medicine will be the medicine of the future.

'p-medicine - From data sharing and integration via VPH ("*Virtual Physiological Human*") models to personalized medicine' is a 4-year integrated project aiming at developing new tools, IT infrastructure and VPH models to accelerate personalized medicine for the benefit of the patient[1]. In p-medicine 19 partners from 9 European countries and Japan, with academic, industrial or clinical background have dedicated themselves to creating, supporting, and sustaining new knowledge and innovative technologies to overcome current problems in clinical research and pave the way for more individualized therapy. The project is co-funded under the European Union's 7th Framework Programme. Beneficiaries of the project represent universities, small and medium sized enterprises, and industry, and comprise stakeholders from IT, basic research, clinical medicine, law and ethics – a variety of expertises conferring added value to the project.

The emphasis of p-medicine is on formulating an open, modular framework of tools, services and infrastructure. It will include efficient secure sharing and handling of large personalized data sets, will build standards-compliant tools and models for VPH research, and will enable multiscale VPH simulations ('*in silico* oncology'). All developed tools, models and services will be open-sourced to allow access by other researchers and end-users, and integration with the VPH-Toolkit is anticipated as well. New technologies, like cloud computing, will be further developed and validated in the cancer domain. Privacy, non-discrimination, and access policies are being aligned to maximize protection of and benefit to patients. The p-medicine tools and technologies will be validated within the concrete setting of advanced clinical research. Pilot cancer trials have been selected based on clear research objectives, emphasizing the need to integrate multilevel datasets, in the domains of Wilms tumour, breast cancer and leukaemia as a test of principle. To guarantee in-time availability of results to clinicians from decision support tools based on models, high performance computing will be explored extensively in the project.

It is a major goal that the developed tools will meet requirements to be used in large, international, multicentre, and good clinical practice-compliant trials. They should be easily integrated into existing infrastructures like ECRIN (European Clinical Research Infrastructures Network) and others. Previous R&D work done in other European funded projects like ACGT, ContraCancrum, TUMOR, CONTRACT, VPH-Share, EURECA, INTEGRATE and ECRIN fits perfectly into this approach and will be heavily drawn upon. Collaboration with the VPH network of Excellence as well with ENCCA (European Network for cancer in children and adolescents) is being fostered.

As p-medicine will explicitly integrate an impressively large number of biocomplexity levels in different cancer types and will address pathogenesis, it might be viewed as the precursor of the "second generation" of Oncosimulators. Beyond that, the direct and orchestrated involvement of cancer hospitals throughout Europe will provide a large number of cases per year for the optimization and validation of the p-medicine IT-infrastructure and tools, which is expected to take *in silico* oncology a big step further.

In developing an innovative and integrated technological solution to enable personalized medicine, the project responds to an urgent societal need. New measurements, modelling and visualization technologies, as well as new computational and mathematical tools, are expected to allow our current, largely reactive model of medicine to be replaced over the next 10 to 20 years by a personalized, predictive, preventive, and participatory medicine.

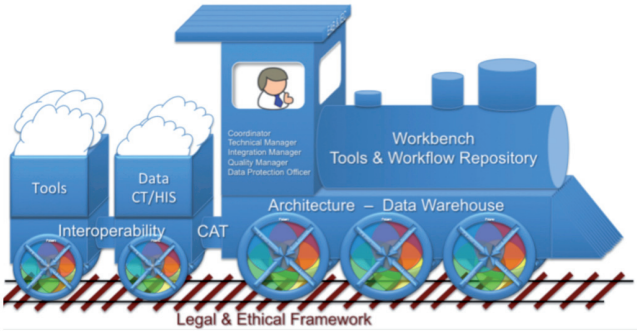

Fig. 1: The p-medicine train, showing the components of the infrastructure project.

It is the final goal of this project to develop the p-medicine environment to a self-sustaining entity that will further develop the vision of this project to foster personalized medicine.

p-medicine aims at creating innovative and integrated technological solutions that will facilitate the translation from current practice to personalized medicine by addressing the following objectives:

- Combine clinical, molecular biological and genomic data in individual patients
- Create a collaborative environment facilitating clinically driven multi-scale VPH modelling
- Deploy clinical trials for VPH adaptation and validation purposes leading to decision support
- Build a data warehouse and p-medicine workbench to run VPH simulations
- Exploit the potential of high-performance computing and cloud storage
- Improve semantic interoperability and data integration
- Increase the quality of data mining in biomedical research
- Establish a service framework for accessing biomaterial resources
- Empower patients through appropriate tools
- Establish the legal & ethical framework
- Link the p-medicine environment with important European Research Infrastructure Initiatives
- Develop training and educational e-Learning tools
- Develop a business plan to further develop p-medicine into a self-sustaining entity

Project coordinator

Saarland University, Germany

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Project website:
http://www.p-medicine.eu

INTEGRATE – p-medicine: Envisaged areas of collaboration

The INTEGRATE and p-medicine projects have engaged a dialogue in order to exploit possible synergies and build on possible joint results. This collaboration will centre on 4 different areas:

User groups

Since the two projects have similar but complementary user groups, one of the objectives of the INTEGRATE and p-medicine collaboration is to cross-validate their respective tools at different stages of development.

Legal framework

The interview of Nikolaus Forgó in the "View Point" section of this newsletter illustrates the efforts already undertaken to bring together the ethical-legal expertise of these two projects. Common issues include data protection, intellectual property rights, contract templates, and use of the Center for Data Protection (CDP, www.privacypeople.org).

Analytical tools

In addition to the "sharing" of user groups, both projects could join forces for the construction of the collaborative environment that they intend to create, more specifically through the reuse of analytical and VPH modelling tools.

Exploitation

Collaboration between the two projects could also take the form of joint dissemination of project results, joint meetings and workshops. Models for exploitation of the project results beyond the duration of the project could also be discussed together. ●

Reference

[1] Project identifier
Contract number: FP7-ICT-2009.5.3 (Virtual Physiological Human - ICT tools, services and specialised infrastructure for the biomedical researcher)
Timetable: February 2011 - January 2015
Instrument: IP

INTEGRATE Participation
in the VPH NoE study

The INTEGRATE Consortium actively participated in the 3rd VPH NoE (Virtual Physiological Human Network of Excellence) study group that took place in Barcelona, Spain, 7 to 11 May 2012.

The organizers invited three groups of world-recognized experts to propose a grand challenge in the area of musculoskeletal, cardiovascular, and oncology research that would be discussed during the event.

This year, it was "requested that these grand challenges would identify each a challenging modelling workflow, a minimum list of "essential" tools known to be necessary, and a list of European research groups that are known to be active in research topics that could benefit from the complete realisation of such workflow". For each challenge a workgroup was formed, "composed by the experts who proposed the challenge, expert developers of software tools identified relevant for that challenge, and by young researchers (PhD students and post-docs) who are conducting research in directions that would take clear advantage by the full realisation of the workflow defined by the challenge." (http://www.cistib.upf.edu/vphnoe-sg3/)

INTEGRATE participated in the session on cancer, co-organized by Professor Norbert Graf (University Hospital of Saarland), and Professor Georgios Stamatakos (National Technical University of Athens). The session brought together top clinical, knowledge management and technology experts who discussed key issues in oncology research and care, addressed the potentially significant role of VPH modelling, shared tools and agreed on future collaborations.

It was a great opportunity for the INTEGRATE Consortium to present our project and make contact with other European researchers active in the VPH area in oncology. We also had the opportunity to demonstrate our first prototype implementing a patient recruitment tool based on the molecular screening scenario of INTEGRATE and to gather feedback from clinical users and from other tool developers. ●

INTEGRATE
discussions in Australia

The INTEGRATE project was recently presented at the 34th Annual Scientific Meeting held by the Australian New Zealand Breast Cancer Trials Group (ANZBCTG), which has been a member of the Breast International Group (BIG) for more than 10 years . The meeting was attended by surgical, medical and radiation oncologists as well as supportive care specialists, oncology nurses, patient advocates and data specialists from all over Australia. Several International key note speakers with expertise in molecular screening and biomarker development presented scientific research data and strategies for future research advancement. The INTEGRATE project objectives; design and timelines were presented at the end of a scientific session on biomarker development and molecular screening. The presentation was extremely well received by delegates and international awareness for the INTEGRATE was raised that could potentially lead to scientific collaborations for data sharing and molecular screening with researchers of the ANZBCTG. ●

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same time, connections between multiple users and the R system are established, with each using their own data space and working directory without interfering with other connections.

INTEGRATE Analysis Platform supports an engine[4] to create dynamically statistical analysis reports by enabling integration of R code and LaTeX documentation[5]. On-the-fly reports are thus generated by combining the program source code and the corresponding documentation into a single file.

To summarize, the INTEGRATE Analysis Platform is being designed to offer intuitive services for the analysis of clinical, genomic and imaging data that will be housed on INTEGRATE. Multiple users will be able to browse through trial data and run simple statistical tests, survival analyses and employ several other clinico-genomic analytical tools. ●

References

[1] Liferay (www.liferay.com)
[2] The R project for Statistical Computing (www.r-project.org)
[3] Rserve, a binary R server www.rforge.net/Rserve
[4] The Sweave tool (www.statistik.lmu.de/~leisch/Sweave)
[5] LaTeX, a document preparation system (www.latex-project.org

Interview
with Prof Forgó

Nikolaus Forgó

In this interview, Nikolaus Forgó, Professor of Legal Informatics and IT-Law at the University of Hannover in Germany, provides us with insight into the legal challenges that underlie clinical research and the secondary use of patient data for research, and the requirements for data protection.

***INTEGRATE:* What is your expertise and what are your fields of interest?**

Nikolaus Forgó: I'm a lawyer. Since 2000 I've been working as full Professor for Legal Informatics and IT-Law at the University of Hannover. My fields of interest are IT law, legal informatics, civil law, legal history and legal theory. I am currently involved in several European Commission projects. We coordinate the CONTRACT FP7 project ("Consent in a Care and Trial Environment") and we participate in several other IT related projects such as p-medicine ("From data sharing and integration via VPH models to personalized medicine»), EURECA ("Enabling information re-Use by linking clinical REsearch and Care") and Linked2Safety ("A Next-Generation, Secure Linked Data Medical Information Space For Semantically-Interconnecting Electronic Health Records and Clinical Trials Systems Advancing Patients' Safety in Clinical Research").

What is the legal framework surrounding the use of health/medical data?

The use of health/medical data is regulated by the European Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, also known as the "Data Protection Directive" and by its national transpositions in the different EU countries. The second relevant directive is the clinical trials directive (2001/20/EC). Both directives are currently under review.

What will the changes be? How will the research environment be impacted?

The major change is that the Directives will be transformed into Regulations, which means that they will be directly transposable into national law. This will allow a more uniform application across countries and thus have direct implications for European research. Besides, both texts will try to foster research by establishing a clearer regime for the need and non-need of informed consent in clinical trials.

The INTEGRATE project aims to develop a data environment and tools for supporting patient enrolment in clinical trials, data and knowledge sharing, and large scale collaboration. We also aim to enable reuse of patient data for clinical research. In this context, what are in your view the key legal and data protection challenges for INTEGRATE?

I can already identify three main challenges: First, the distinction between the primary use and secondary use of data will be relevant as two different legal regimes apply (care on the one hand, research on the other hand). Second, it will be difficult to distinguish whether the data is to be considered as personal data – for which the data protection legislation applies – or anonymised. The frontier between the two is very thin as in some case you can trace back anonymised data. Finally, in a project such as INTEGATE, the question of data access by third parties is going to be crucial. This issue is intrinsically linked to exploitation questions.

How are patients protected with regards to the processing of their personal data?

There are three principles underlying the right of patients in terms of use of personal data for research purposes: The first principle is that patients have the right to be informed about which of their data are going to be processed, by whom and for which purpose. Secondly, they have the right to withdraw their consent at any time. This requires that data can be tracked (but this is not possible in case of fully anonymised data) and deleted. Thirdly, patients must have the possibility to correct their data if needed.

Is the growing public awareness of clinical trials a threat for research?

On the contrary. The more patients know about clinical trials, the more they will be inclined to support research by contributing their data. Legislators need to be pragmatic and find the right balance between the necessity of protecting the rights of the patients and the necessity to promote health research.

What are the challenges or restrictions with respect to secondary use of electronic health record (EHR) data for research?

The recording of patient data into EHR does not necessarily require informed consent. However the secondary use of this EHR data does so in most cases. It is therefore more practical to start by asking this consent at the time you are creating the EHR. And asking this type of consent is always a challenge. The request must be based on a description that is broad enough to cover research questions that are not yet identified at the time of the consent, but narrow enough so that the patient still knows what she/he is consenting to.

INTEGRATE aims to build a data sharing environment that will aggregate comprehensive datasets from clinical trials to be used for future research. What are the legal challenges with respect to reusing the data collected within clinical trials for future research?

It would depend on the consent given. Investigators have to bear in mind that a consent that is too broad does not cover

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INTEGRATE
participants and their teams

This section is dedicated to the presentation of the INTEGRATE participants and their teams. For this first issue, focus is set on Custodix and FORTH.

Custodix is a Belgian private limited company established in 2000 that specializes in data protection solutions primarily for eHealth and clinical research. Today Custodix is recognized as one of the most advanced and reliable Trusted Service Providers (TSPs) in the healthcare sector.

Custodix offers privacy protection and security services for data management, including de-identification, Identity and Access Management, Public Key Infrastructure and time-stamping; additionally it provides managed services to customers dealing with sensitive data. Furthermore, because of its expertise in the clinical domain, Custodix is often engaged as custom IT solutions provider for projects in the life science domain.

Since its founding, Custodix has been involved in several European research projects (FP5, FP6, FP7, IMI), including ACGT (Advanced Clinico-Genomic Trials on Cancer, 2006-2010). TAS3 (Trusted Architecture for Securely Shared Services, 2008-2011), EHR4CR (Electronic Health Records for Clinical Research, 2011-2014), EURECA (Enabling information re-Use by linking clinical REsearch and Care, 2012 - 2015) and INTEGRATE.

Customers are both commercial companies (pharmaceutical companies and data brokers) and governmental organizations.

Brecht Claerhout

Brecht holds a master degree in electronics engineering. He has previously been active in FOSS development as author of a major network security tool (Sniffit). He has worked at the Interuniversity Microelectronics Center (IMEC) () and Research in Advanced Medical Informatics and Telematics (RAMIT) () research groups. Brecht is currently leading R&D at Custodix and has been actively involved in a large number of European research projects (mainly dealing with the health data integration). Recent projects include ACGT, TAS3, EHR4CR, EURECA and INTEGRATE.

Kristof De Schepper

Kristof holds a bachelor in Informatics and a master in Computer Science specialization Software Engineering from the University of Ghent. He started working for Custodix two years ago, where he combines the roles of researcher, software developer and architect. Apart from the INTEGRATE project, he has also been active in other FP7 projects like EURECA and TAS3.

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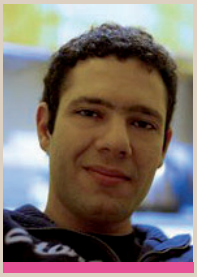
secondary use. Asking for consent for the use of personal data "for future research" purposes is not allowed from the ethical-legal point of view. An alternative would be to anonymise the data. In the context of international data sharing for research purposes and when the data is coming from different countries another important factor is where the data is stored. This has direct implications on the way the data must be treated.

With the increasing use of online tools for patient stratification and treatment selection that require the input of all the relevant patient data, what are the risks with respect to privacy and data protection? What data can be provided in such tools before there is the risk that the patient becomes identifiable?

The rule is that the clinical data (age, sex, clinical values, diagnostics values etc.) entered in the system may not make it possible to identify the patients. If it is plausible that someone is able to identify the patient by using reasonable means, then the data should be considered as personal and consent is required in principle. ●

The Foundation for Research and Technology – Hellas (FORTH) is one of the largest research centres of Greece with well-organised facilities and a highly qualified staff. The research and technological focus of the foundation is centred on selected areas of great scientific, social, and economic interest. The Institute of Computer Science (ICS) with the Computational Medicine Laboratory (CML) is involved in and contributes to the INTEGRATE project. ICS, since its establishment in 1983, is a pioneering contributor towards the deployment and adoption of Information Society Technologies in Greece and plays a leading role in worldwide efforts towards the development of an Information Society accessible and acceptable by all citizens. The CML lab at ICS-FORTH has established a tradition of internationally acknowledged excellence in conducting high-level R&D work and in developing innovative systems and services. Its research activities focus on the development of innovative computer methods and tools in the area of medical and biomedical informatics, eHealth, m-Health, medical imaging and bioinformatics. Recently the lab has also been focusing its R&D activities on biomedical modelling and simulation in the wider VPH research context.



Ioannis Karatzanis

Ioannis is a Computational Physicist with experience in graphical user interface design and in development of both web and native applications mostly oriented to the medical field and education. In the education field, he has been an active developer and multimedia designer of the Multimedia Lab for five years, in the department of Physics of the University of Crete, where in cooperation with the «Crete University Press», created a series of interactive lessons of physics (available in CD/DVD and also online). He participates in a number of EC projects including INTEGRATE, Reaction, ContraCancrum and TUMOR. In the INTEGRATE project he is responsible for the user interface, the user experience and the core functionality for both the analytical tools and the central review for pathology images, and finally for their unification under a common environment, using as a basis the Liferay platform.

Georgios Manikis

Georgios received a Master's degree in electronics and computer engineering from the Technical University of Crete, Greece. He currently works with the CML at ICS-FORTH. He has been working on various national and European projects as a research assistant and software developer. His research interests are in the areas of medical image processing, modelling of biological processes, biostatistics and pattern recognition with applications in classification, feature extraction, and data integration.

Kostas Marias

Kostas holds a Principal Researcher position ICS-FORTH. He completed his PhD in the field of Medical Image Analysis/ Medical Physics in 2001 (UCL London, Royal Free Hospital) working in the Medical Vision Lab, University of Oxford. Recently he coordinated the ContraCancrum EC project on cancer modelling and is actively participating in the TUMOR, p-medicine and INTEGRATE projects developing open access image analysis/modelling tools for the promotion of predictive medicine within the wider VPH EC initiative. Within INTEGRATE he works on the analytical tools and predictive modelling mainly from the imaging biomarker perspective.

Manolis Tsiknakis

Manolis is an Associate Professor of Biomedical Informatics and eHealth, Department of Applied Informatics and Multimedia at the Technological Educational Institute of Crete and an Affiliated Researcher to ICS-FORTH. He received his PhD in control systems engineering from the University of Bradford, UK. He has coordinated many collaborative EU funded research projects. Recently, Manolis has been the scientific coordinator of an EU funded integrated project (ACGT - Advancing Clinico-Genomic Trials on Cancer) focusing on the development of innovative ICT solutions supporting large scale translational research on cancer. He is also involved in a series of R&D projects in the domain of cancer biomarker discovery and translational medicine, like p-medicine, ENCCA, and INTEGRATE. He is the initiator and co-chair of the ERCIM Biomedical Informatics Working Group. He is the team leader of FORTH within the INTEGRATE project.

Events & Publications

Past

INTEGRATE Technical Meeting,
Madrid, Spain,
10 – 11 January 2012

INTEGRATE Consortium Meeting,
Gent, Belgium,
6-8 February 2012

INTEGRATE Technical Review Meeting,
Brussels, Belgium,
2 May 2012

INTEGRATE Consortium Meeting,
Brussels, Belgium,
26 – 27 June 2012

Upcoming

INTEGRATE Consortium Meeting,
Madrid, Spain,
1 – 2 October 2012

INTEGRATE Consortium Meeting,
Brussels, Belgium,
5 – 6 February 2013

INTEGRATE Consortium Meeting,
Gent, Belgium,
11 – 12 June 2013

Intergroup Plans for Managing Biomarker Research – the B.I.G. Program, ANZBCTG Annual Scientific Meeting, Hobart, Tasmania, Australia,
20 July 2012

1st INTEGRATE Workshop,
17th ECCO – 38th ESMO – 32nd ESTRO European Cancer Congress Amsterdam,
The Netherlands,
September 2013

Recent publications

Perez-Rey D, Jimenez-Castellanos A, Garcia-Remesal M, Crespo J, Maojo V. **CDAPubMed: A browser extension to retrieve EHR-based biomedical literature.** *BMC Medical Informatics and Decision Making 2012, 12:29.* 5 April 2012
http://www.biomedcentral.com/1472-6947/12/29/abstract

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SEVENTH FRAMEWORK PROGRAMME

European Commission
Information Society and Media

eHealth
Better Healthcare for Europe

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