PROJECT PERIODIC REPORT

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Project acronym: OraMod

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Funding Scheme: ICT-2013.5.2 Virtual Physiological Human

Physiological Human

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Periodic Activity Report: **1st** ☑

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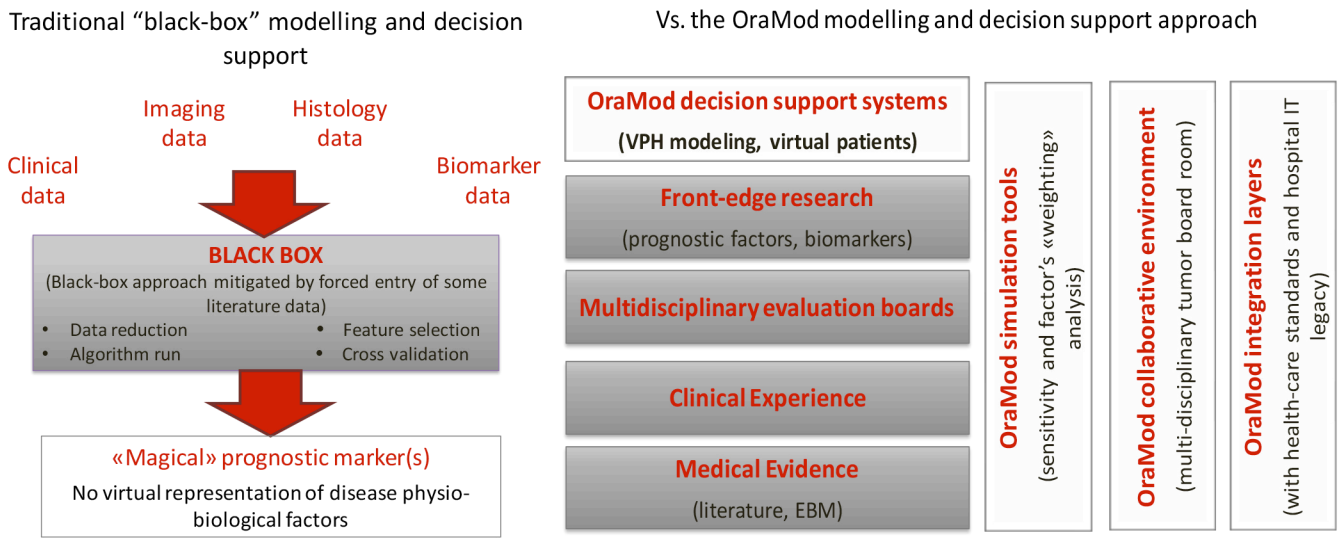
PUBLISHABLE SUMMARY

Cancer patients management involves critical decisions, regarding best treatment to avoid disease reoccurrence, to ensure the most favourable prognosis, to avoid over-treatment but at the same time also prevent under-treatment and - mostof all - to preserve the quality of life for patients. This decision making process starts at the time of diagnosis and - besides personal experience and knowledge of best practices - it involves an in-depth understanding of the disease presentation in each specific patient. OraMod starts from the need of researchers and clinicians in the field of oncology to improve the representation of biological processes related to growth, dissemination and reoccurrence of cancer, with the aim to predict disease prognosis and to provide effective and personalized care. This poses some challenges, both methodological and technical: to effectively represent the multi-scale biology of the disease and to translate predictive models into clinical practice.

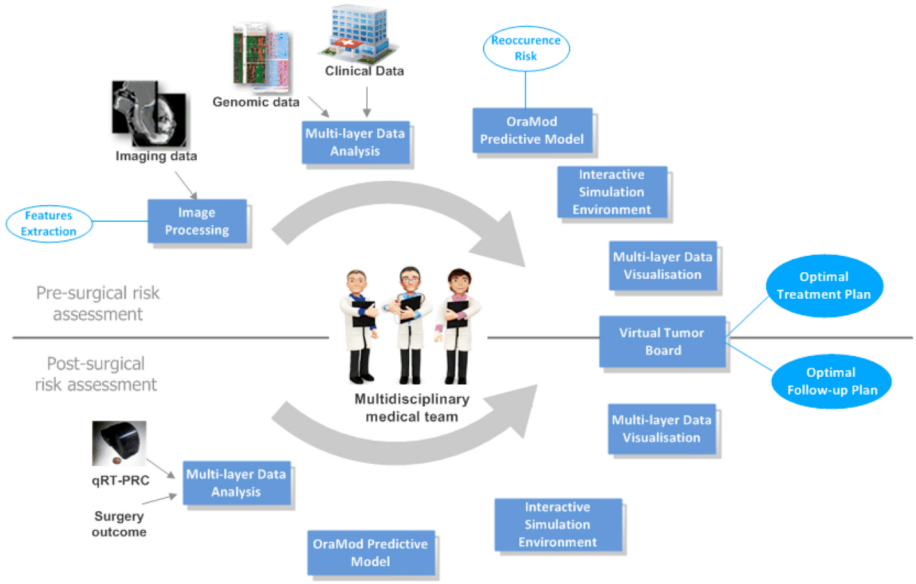
The systemic nature of cancer impacts all levels of human physiology, from molecular levels up to organs and the entire organism. Traditional data visualization technologies, are not able to address this complexity and combine visual representations of the different levels of physiology into a unified vision of the disease, and of the disease presentation in each individual patient. The multidisciplinary decision-making required to address cancer also needs that this wealth of data and its interpretation by means of predictiove modelling (risk models) is shared among the clinical team (tumor Board).

On the other side, the nature of predictive models makes them obscure to clinicians, who see them as "black-boxes", which produce some "magic" prediction and some "dont't know where they come from" predictive markers. The clinical decision maker has no control over these factors and their weight, and has no clear vision of what adds to current practice. This lack on insight into the factors that contribute to define the prediction has so far prevented the adoption of models into the clinical practice.



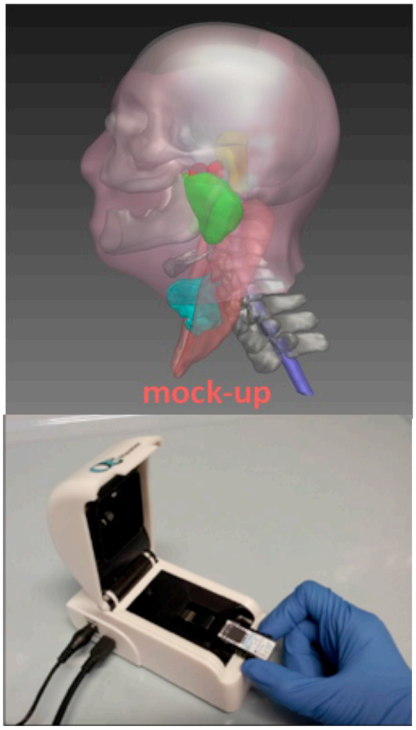
OraMod has the ambition to overcome these drawbacks,as it intends to:

1. Implement visual representations of the bio-phisiology factors involved in oral cavity cancer onset and evolution, personalized to the different views required by the multidiscinplinary teams of specialists involved in oral cancer management, in the frame of a "Virtual patient" representation concept, as foreseen by the Virtual Physiological Human vision.
2. Realize a predictive model which is built on current knowledge as an incremental tool (i.e. adding incrementally predictive factors from different levels of disease physio-biology), is "transparent" in terms of predictive factors and their relative weight, and reduces the intra-observer variability of data interpretation.
3. Foster a collaborative case management and a multidisciplinary treatment approach through patient's data sharing and presentation (the Virtual tumor Board) tool.



OraMod approach, relying on secure integration of huge health datasets, medical knowledge, multi-disciplinary collaborative best clinical practices and cutting-edge technologies, including modelling and in-silico simulation, will improve (1) the multi-specialist approach to diagnosis, risk assessment, and treatment decisions and (2) the integration of research-derived evidences into the clinical practice (i.e. the evidence-driven approach).

A longitudinal pre-clinical trial on Oral Cavity Cancer, involving more than 400 cases (retrospecive and prospective) will demonstrate the effectiveness of the model to improve clinical decisions and will estimate the socioeconomic impacts and benefits for patients, clinicians, and all the healthcare ecosystem concerned with oral cancer management.



The core of OraMod platform is the predictive model, which will be integrated into a web-based modular framework of tools, services and diagnostic devices supporting clinical decisions. They include:

i. a highly interactive *Knowledge Assisted Visualization and Simulation* environment for the "virtual" presentation of patients' data, in line with the "Digital Patient" concept,

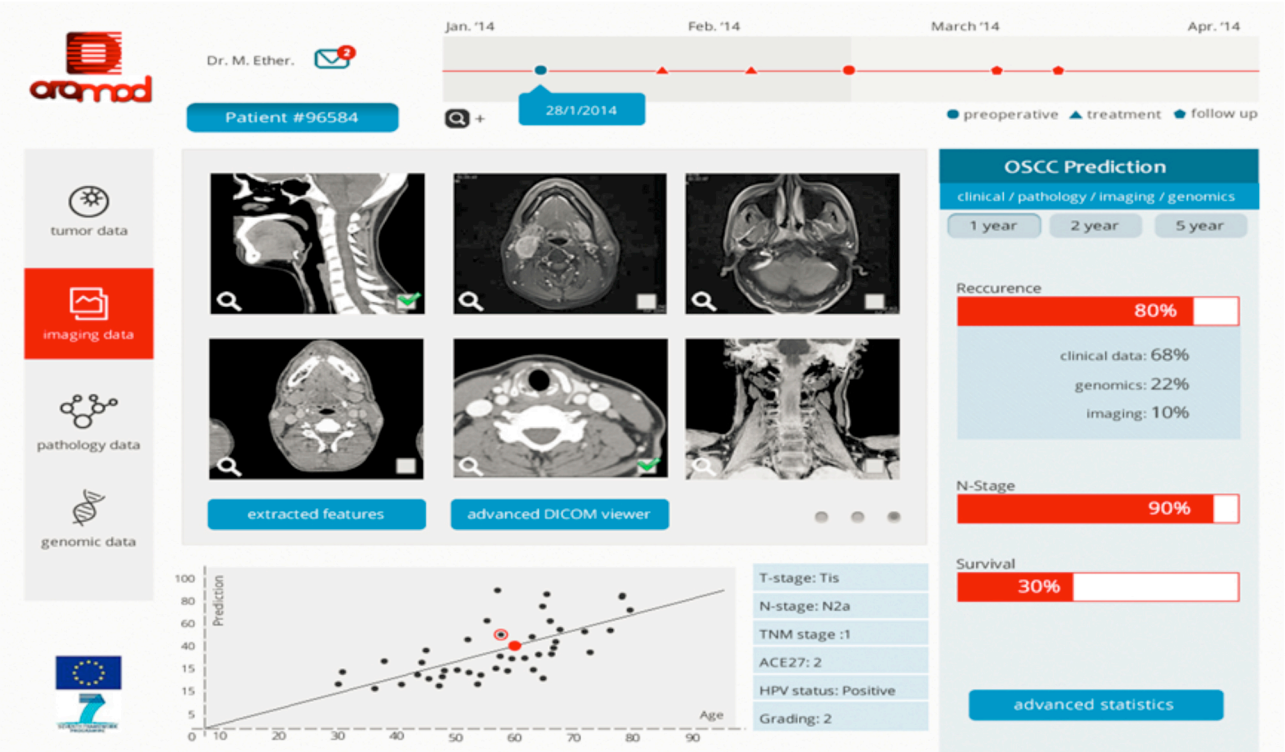
ii. a *collaborative decision-making space*, the "Virtual Tumour Board", to support the multi-disciplinary approach through the interaction of the different specialists concerned with treatment decisions,

iii. a sophisticated suite for *image analysis and feature extraction* for head and neck diagnostics, and

iv. a portable *RT-PCR device and a disposable personalized lab-on-chip* for fast, precise, quantitative detection of the genomic markers included in the prediction model.

These tools will allow the collection and presentation of the multiscale data related to oral cancer patients, which will be used to build, by means of the OraMod model, a fingertprint of each patient's disease progression and to stratify each patient by risk of disease reoccurrence, lymph-nodes metastases and overall survival.

The project has currently concluded the design phase: user needs and use cases have been defined, the clinical protocol approved by the Ethical Committees in the three involved hospitals (Head & Neck Department of Parma University hospital, VUmc Medical Centre Amsterdam, Heinrich-Heine University hospital Dusseldorf) and in three associated clinics in Germany. Patients are being enrolled and data and biologic samples collected and analysed, along with diagnostic images. The technical development has progressed with the first release of the OraMod documentation system (i.e. the electronic health records), the genomic profile detection and evaluation algorithms. The user interfaces mock-ups are being validated by users and the data entry system is expected to be ready for usage by the end of October 2014.



The Consortium has started dissemination by addressing the medical and scientific community in specific events (EACMFS congress Prague, SPIE 2014, IEEE EMBS BHI 2014 in Valencia). More events and actions are expected in the next months.

The Consortium has already started a survey of possible exploitation opportunities for the OraMod platform and for individual components (i.e. Image Analysis Tools, RT-PCR and lab-on-chip). Market analysis is ongoing, in parallel with the definition of a roadmap for products certification as medical devices and in-vitro-diagnostic devices.

More incisive actions to involve stakeholders and potential targets for market exploitations will be performed in the next months, with the support of the OraMod platform prototype and evidence-based data to demonstrate the added value and the impacts of OraMod for supporting clinical decisions on OSCC patients management.

The project is progressing according to the foreseen plan and using the resources available in line with the efforts devoted and the results achieved.

VPH based predictive model for oral cancer reoccurrence in the clinical practice

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