The ONCOSIMULATOR is at the same time a concept of multilevel integrative cancer and (treatment affected) normal tissue biology, an algorithmic construct and a software system which aims at supporting the clinician in the process of optimizing cancer treatment by performing individualized in silico experiments.

Other envisaged application areas of the oncosimulator:

- Basic science (dynamic integration of multilevel biodata and biomechanisms, in silico experimentation)
- Design of new clinicogenomic trials
- Medical education
- Education of interested patients and/or parents

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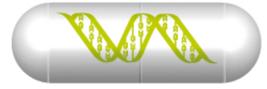
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THE ONCOSIMULATOR

PERSONALIZED
THERAPY



ACGT is in line with ethical guidelines and data protection rules PROJECT N° FP6-2005-IST-026996



## Functioning of the «Oncosimulator» following its thorough clinical validation

## First step: obtain patient's specific data

The following sets of data are collected for each patient:

- · Clinical (age, eventual previous treatments etc.)
- . Imaging (images of MRI, ultrasound, PET, CT etc.)
- · Histopathological (histopathology slide images whenever biopsy is allowed and feasible)
- Molecular (specific molecular marker values and/or DNA array data based on biopsy and/or blood samples)

## Second step: preprocess patient's data

The data collected are preprocessed in order to take an adequate form allowing their introduction into the "Oncosimulator." For example the imaging data are segmented, registered, interpolated, 3-D reconstructed. Similarly the molecular data are combined via molecular interaction networks in order to perturb the average pharmacodynamic or radiobiological cell survival parameters and so on.

## Third step: describe candidate therapeutic schemes

The clinician describes a number of candidate therapeutic schemes to be simulated in silico i.e. on the computer.

## Fourth step: run the simulations

The tumour growth and therapy response computer code is executed on distributed GRID computational resources so that several candidate treatment schemes incorporating many possible unknown tumour parameter values combinations are simulated concurrently. Predictions concerning the toxicological permissibility of each candidate treatment scheme are also produced.

## Fifth step: visualize the predictions

The expected reaction of the tumour as well as indications of the toxicological side effects for all scenarios simulated are visualized using several techniques ranging from graph plotting to virtual reality rendering.

## Sixth step:

## evaluate the predictions and decide on the optimal scheme to be applied

The Oncosimulator's predictions are carefully evaluated by the clinician by taking into account their logic, education and even experience. If no serious conflicts are detected, the predictions can be used to support the clinician in taking their final (expectedly optimal) decision on the actual treatment of the patient.

## Seventh step:

## apply the optimal therapeutic scheme and further optimize the Oncosimulator

The expectedly optimal therapeutic scheme (schedule) is applied on the patient. In parallel the prediction vs. reality comparison data are collected and used as a continuous optimization feedback to the Oncosimulator.

