Multiscale Modeling Clinical and Translational Issues: a multidiciplinary perspective

B.Bass and M.Garbey

Some NIH Definition

"Translational research includes two areas of translation. One is the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans. The second area of translation concerns research aimed at enhancing the adoption of best practices in the community."

From Wikipedia

Translational science is a cross disciplinary scientific research that is motivated by the need for practical applications that help people. The term is used mostly in the health sciences and refers to things like the discovery of new drugs that directly help improve human health. Thus, translating bench science to bedside clinical practice or dissemination to population-based community interventions.

Increasing Range of Difficulties

- Translating Bench Lab.
- Translating “Ordinary Global” Model and Benchlab
- Translating Multiscale Model and Benchlab:
  - Does the experiment should address each scale
  - What is a good data set in that context.
- Designing the pilot study:
  - Is there a good animal model ?
  - How to control/reduce the complexity for a human clinical trial ?
- Getting Multiscale Modeling accepted in the health community.

Companion Concept: Verification and Validation

- Verification: Computing the Right solution of the equation
- Validation: Solving the Right equation

V&V is more difficulty for multiscale modeling!

Multiscale models may imply a large set of parameters to calibrate

Added Value of Multiscale Modeling in Clinical and Translational Research

- Qualitative: bring to light new critical variable:
  - Provide an explanation for failure
  - Gives Target for improvement
- Quantitative: provide better accuracy in prediction
  - Personalized medicine: example of AAA rupture
  - Scalability in Clinical conditions: flops+data acquisition ?
- All this requires new data and raise new funding issue.

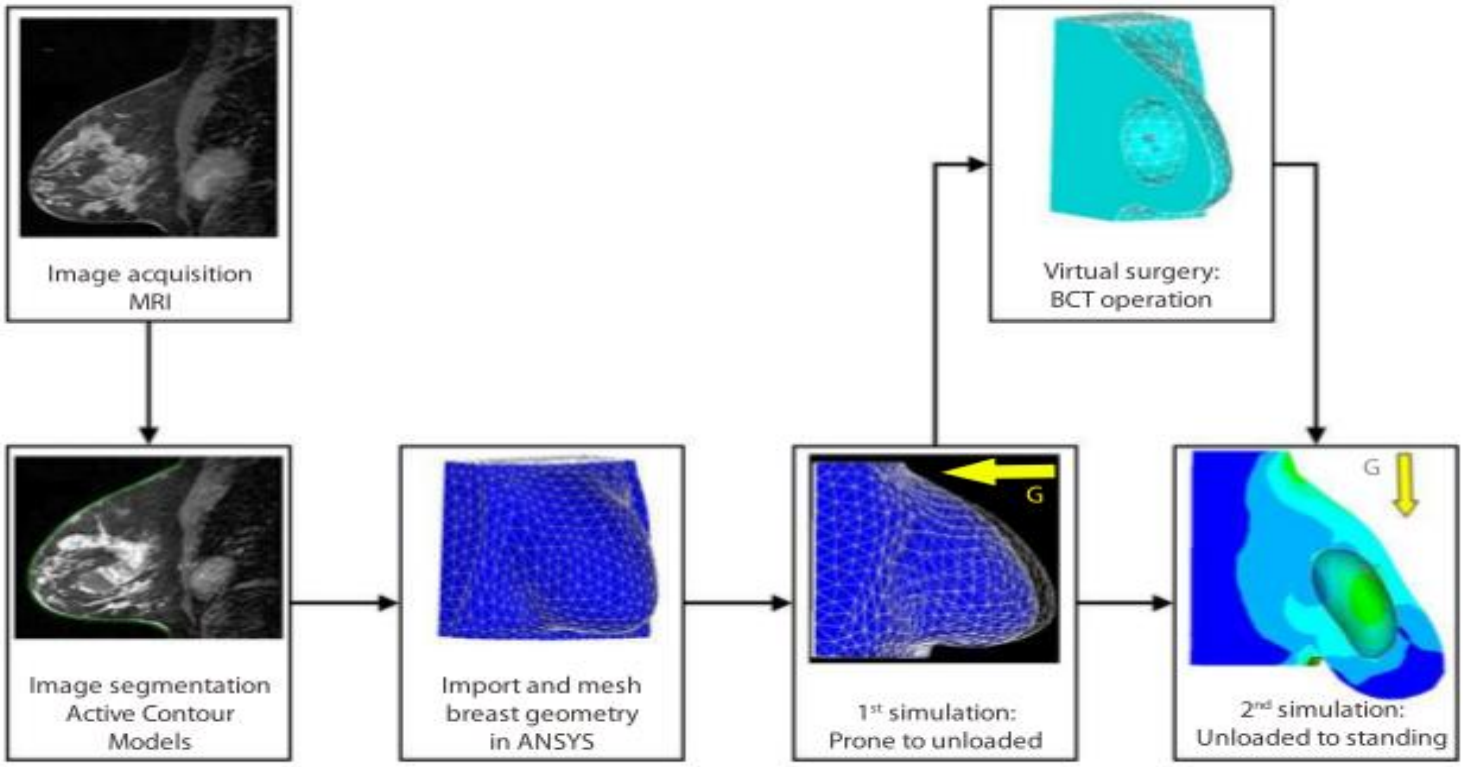
Breast Conservative Therapy

- No Animal Model
- Modern Medicine: this is about quality of life!
- 200 000 new cases per year, that can be cure by BCT thanks to systematic screening and early detection
- We know that multiscale modeling is needed to predict cosmetic side effect and inform patients .
- This is not a minor problem: 30%-40 % range

Goal

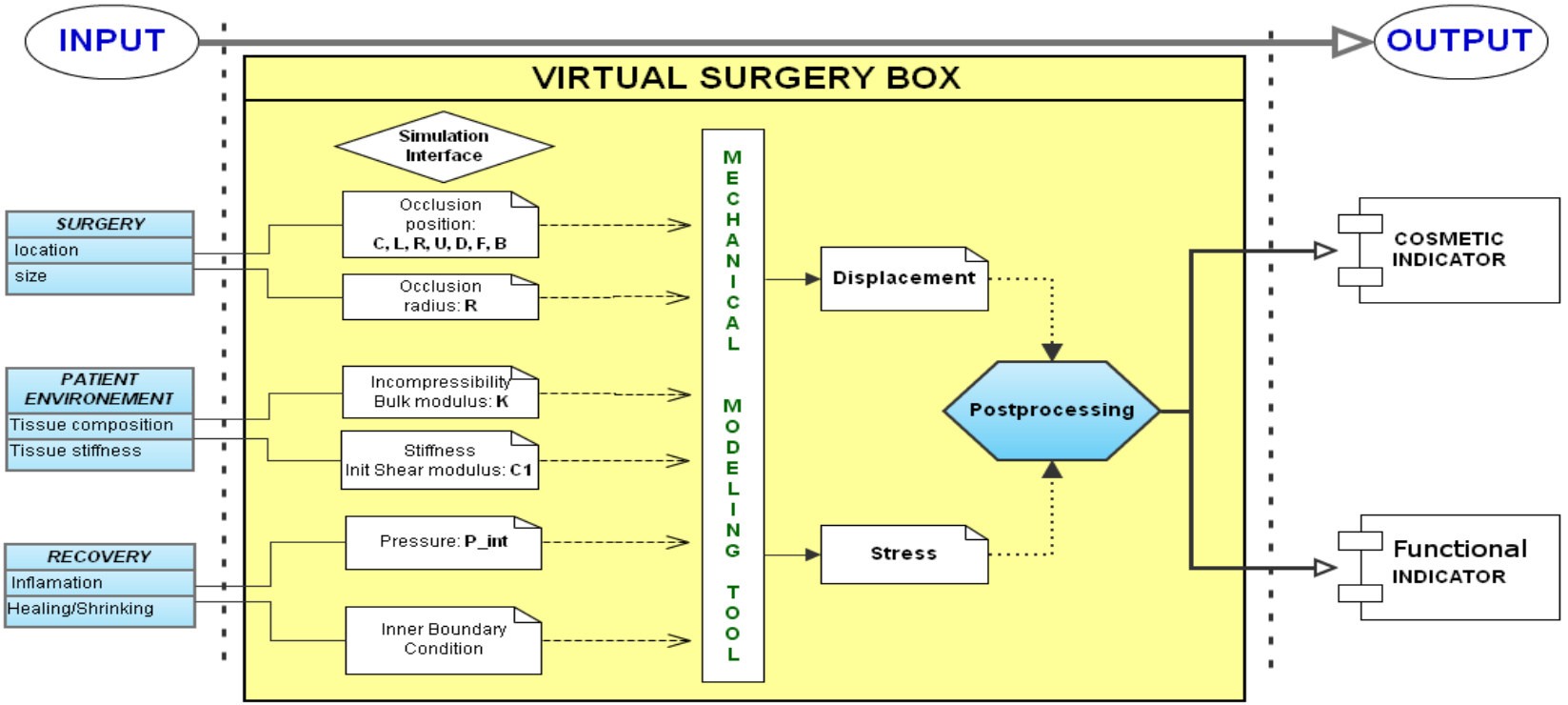
- Improve our ability to predict breast contour and cosmesis in breast conservative therapy.
- To allow our patients to make better informed decision regarding treatment choices.
- To identify opportunities for tissue engineering solutions

From Data Acquisition to Mechanical Modeling



Data is acquired from MRI images. Each slice is segmented using an unsupervised active contour method to retrieve the shape of the breast. The MRI slices are interpolated and meshed in 3 space dimensions to model the breast. The mechanical model use finite element simulation to get the shape of the breast under gravity.

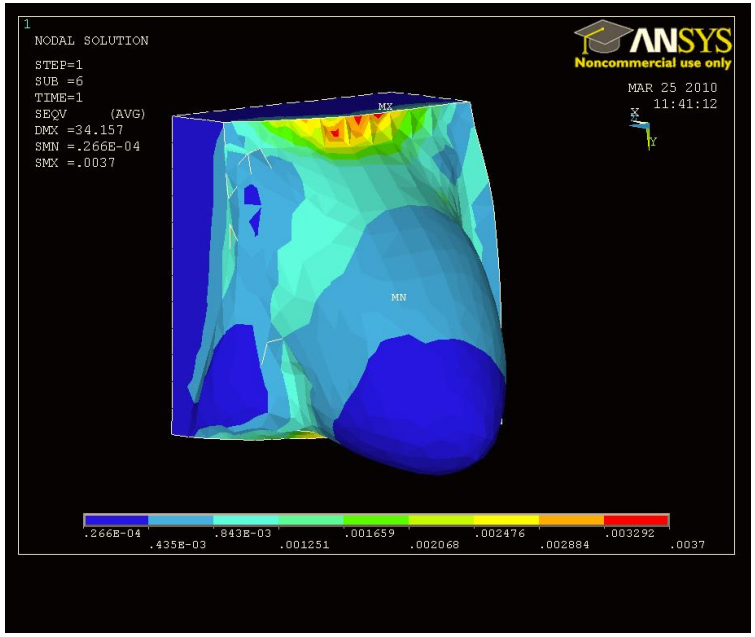
Virtual Surgery Box



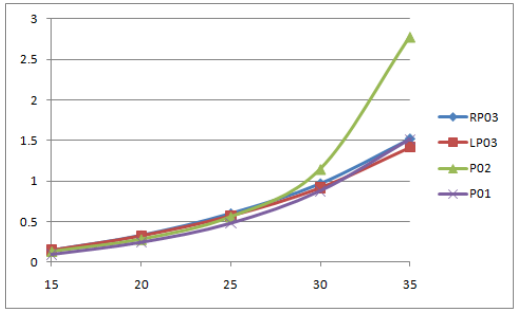
The virtual surgery box was developed as a practical tool for surgeons. It acts as a black box where the input is kept simple and the output contains relevant indicator. Indicators for the global comesis of the breast are used to evaluate the impact of the BCT on the quality of life of the patient.

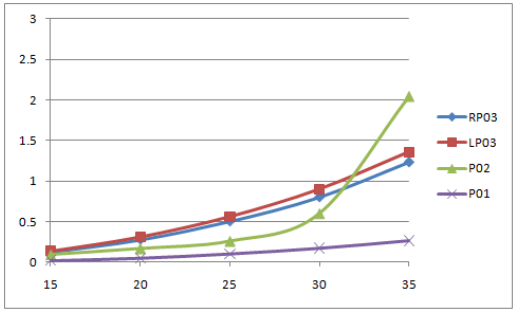
The virtual surgery box aims to be modular and extensible with additional mechanical and/or biological models in the simulation.

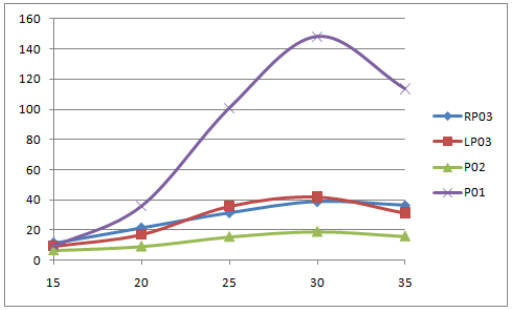
Cosmetic Indicators



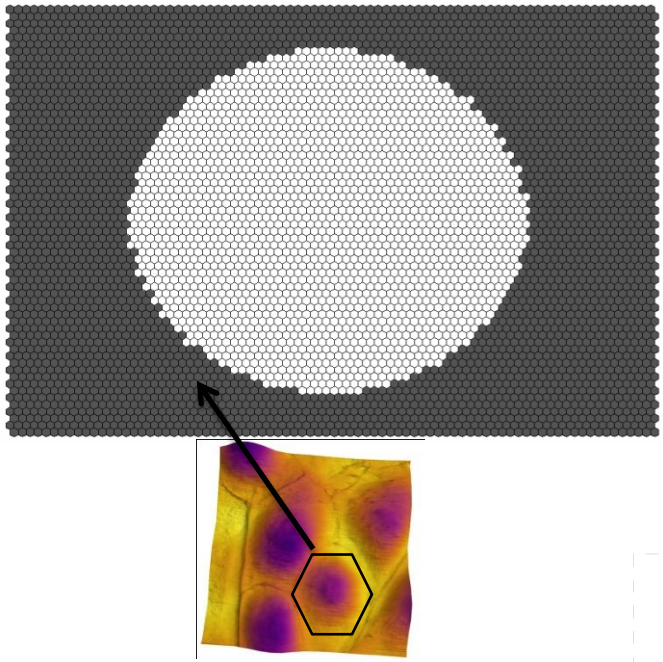
For a patient-specific study we define two indicators that can be used as criterions by the surgeon to evaluate the outcome of the BCT. The cosmetic indicator defines a new metric between the geometry of the breast before and after the BCT while the functional indicator focuses on the localization of the stress. We can compute this indicator as a function of the tumor resection size in both sagittal and axial plan (graph 1,2: cosmetic indicator) or as a function of the tumor resection radius (graph 3: functional indicator).

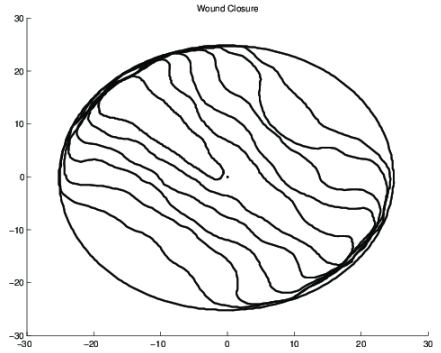


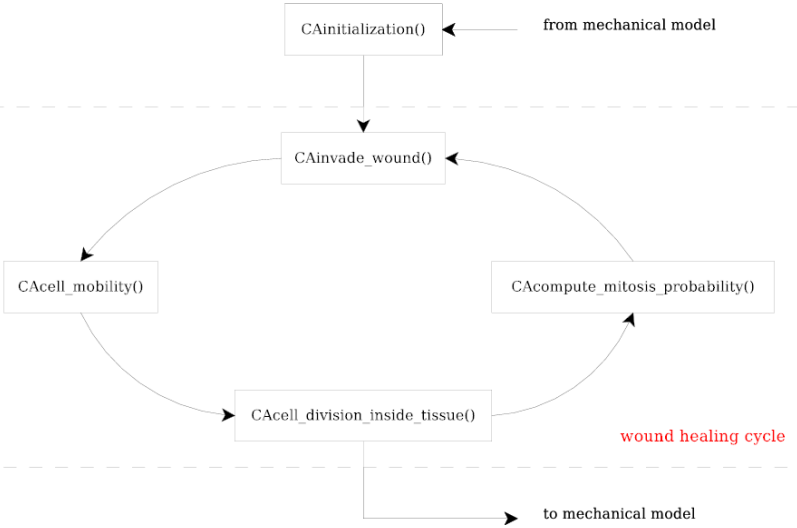




Agent Based Model at the Cell Level



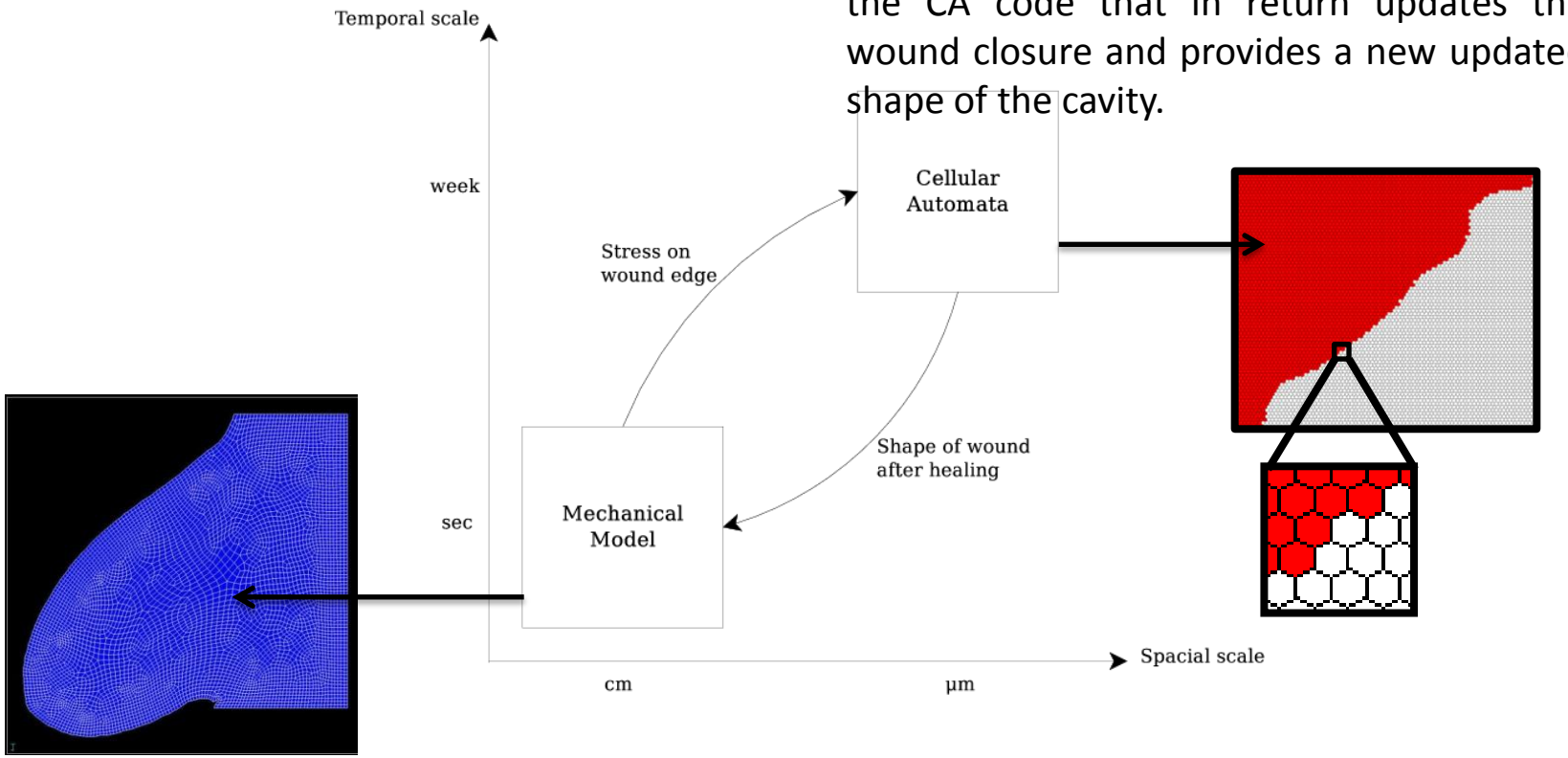




An hexagonal grid is used to model the array of cell of the agent-based model. A limited number of simple rules are repeated to model the wound healing process which takes into account the geometry of the wounded area as well as the strain energy of the breast.

Parallel Multiscale Model

The mechanical model that runs on a multicore PC server is coupled to the CA algorithm that runs on a 1434 cores SiCortex system. The code is written in C and parallelized with MPI. The mechanical model provides the strain energy and geometry of the wound edge to the CA code that in return updates the wound closure and provides a new updated shape of the cavity.



To Build a Pilot study ?

- Thinking out of the Box:
  - We build our own cost stereotactic system.
  - Use of thermal Imaging to monitor Inflammation.
- Using medical imaging systems that have no side effect:
  - 3D ultrasound imaging
  - MRI ….
  - More …
- Building a data base that integrate disparate data set: questionnaire on QOL, Images, Video, Lab Exam etc…
- Modular Design of the Multiscale code: tissue mechanic deformation, wound healing, radiotherapy model, environment conditions model…