

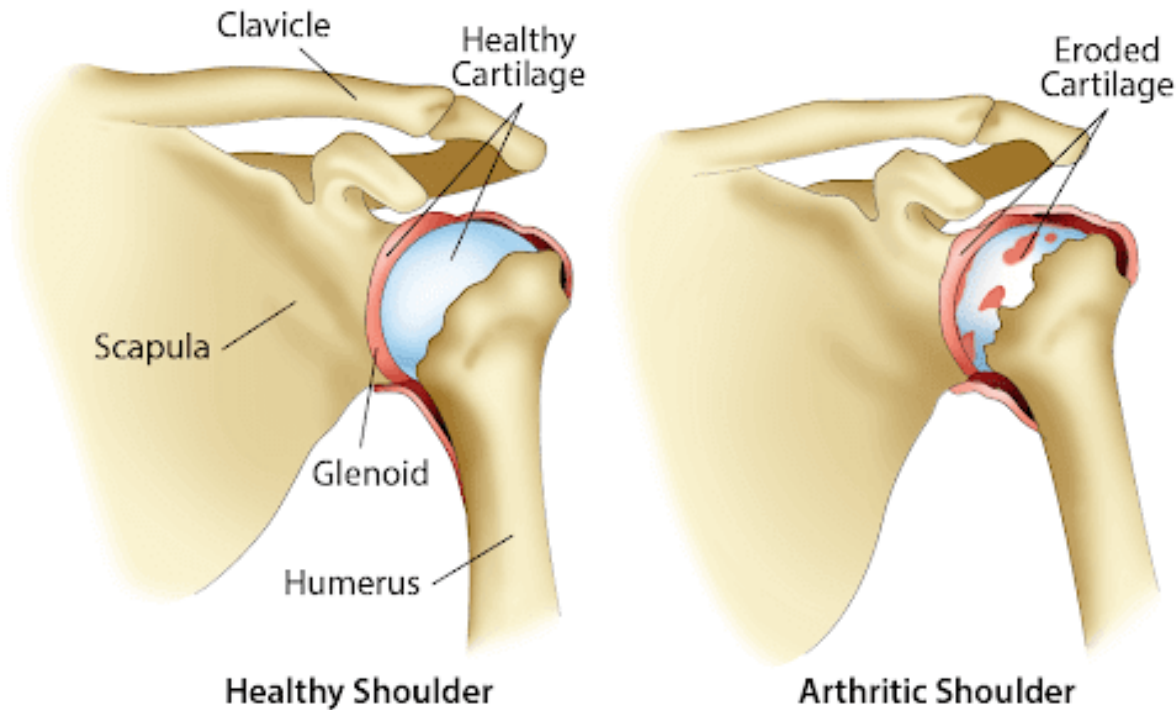
Personalized Biomechanics: Computational Modeling & Simulation for Total Shoulder Arthroplasty

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(EPFL-LBO)

Overview

- Clinical background
- Research methods (LBO experience)
- Clinical, Cadaveric, Modeling
- MusculoSkeletal Modeling
- Finite Element Modeling
- Deep-Learning Modeling
- Populated models
- Causal Bayesian statistics
- Conclusions

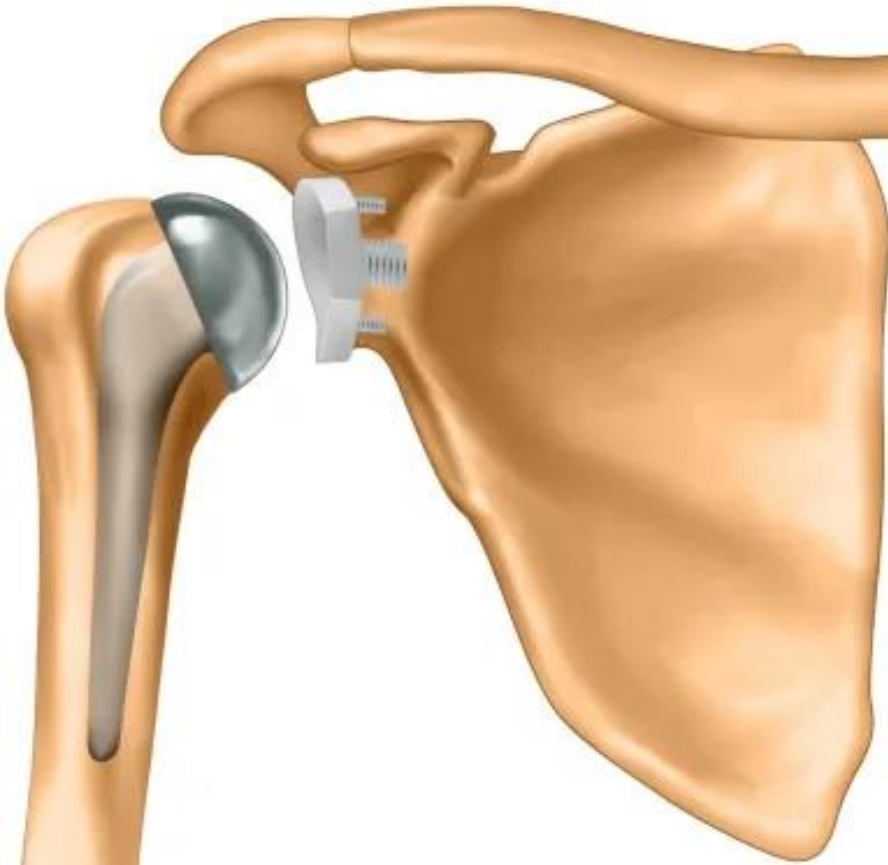
Clinical background: joint degeneration



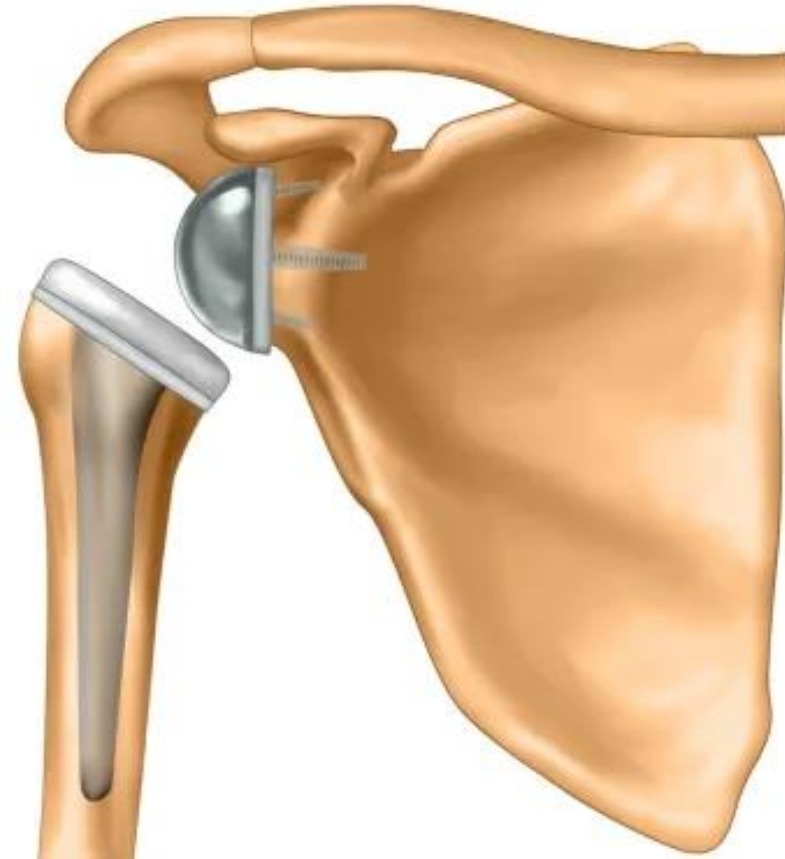
- Osteoarthritis (OA) world's most common joint disease
- Currently no cure
- Glenohumeral osteoarthritis (GHOA) accounts for 5%–17% of patients with shoulder complaints
- Etiology of GHOA is multifactorial

Clinical background

Anatomic Total Shoulder Arthroplasty
(ATSA)



Reverse Total Shoulder Arthroplasty
(RTSA)



Complications of Shoulder Arthroplasty

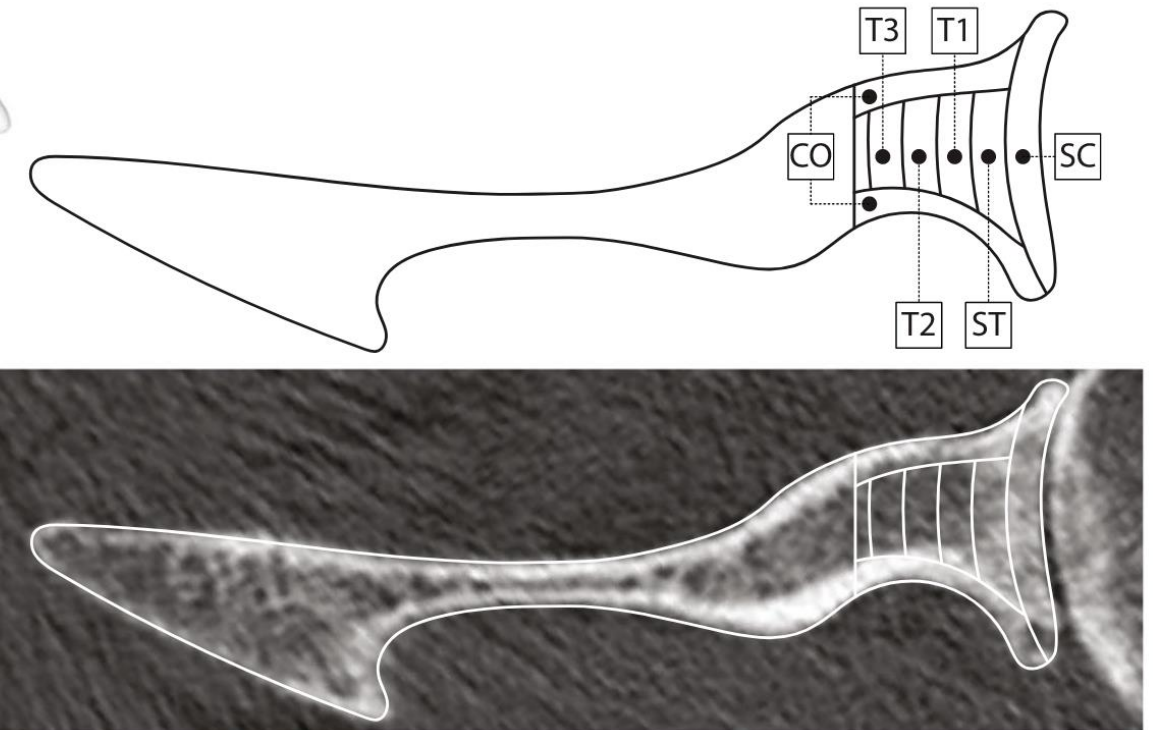
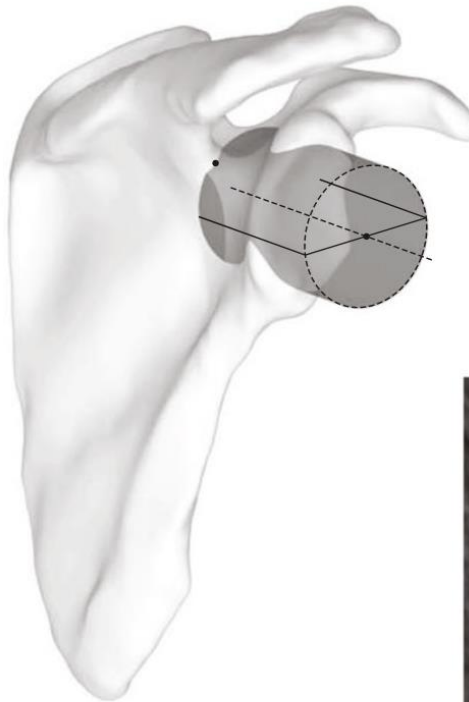
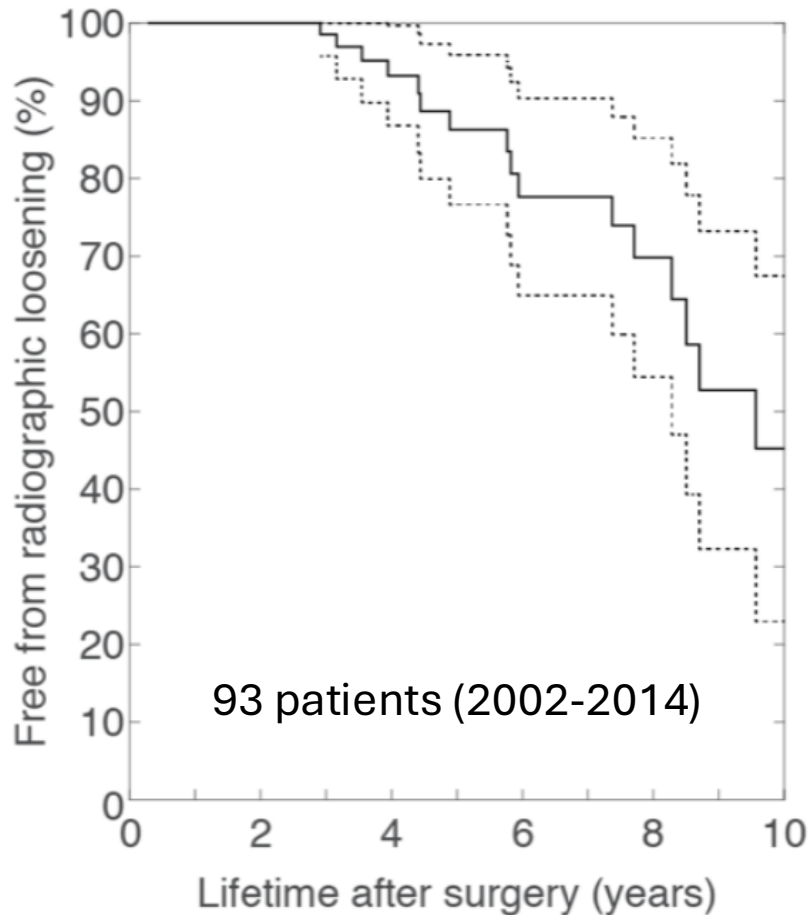
- Meta-analysis of Bohsali et al. (2017)
 - 2006 - 2015, 122 studies, mean follow-up 40.3 months
- ATSA (3360 cases)
 - Complication rate: 10.3%
 - Most frequent: component loosening, glenoid wear, instability
- RTSA (4142 cases)
 - Complication rate: 16.1% for RTSA
 - Most frequent: instability, periprosthetic fracture, infection

Methods to understand/reduce complications

- Clinical trials (randomized multicenter double-blind)
 - Strongest evidence, but time-consuming and expensive
- Cadaveric experiments
 - Realistic anatomy and biomechanics, but not cheap, not clinical reality
- Numerical modeling
 - Fast, cheap, control all variables, but simplification, validation
- In-silico trials
 - Same as above +
 - Personalization, ethical, but requires a lot of (high-quality) data

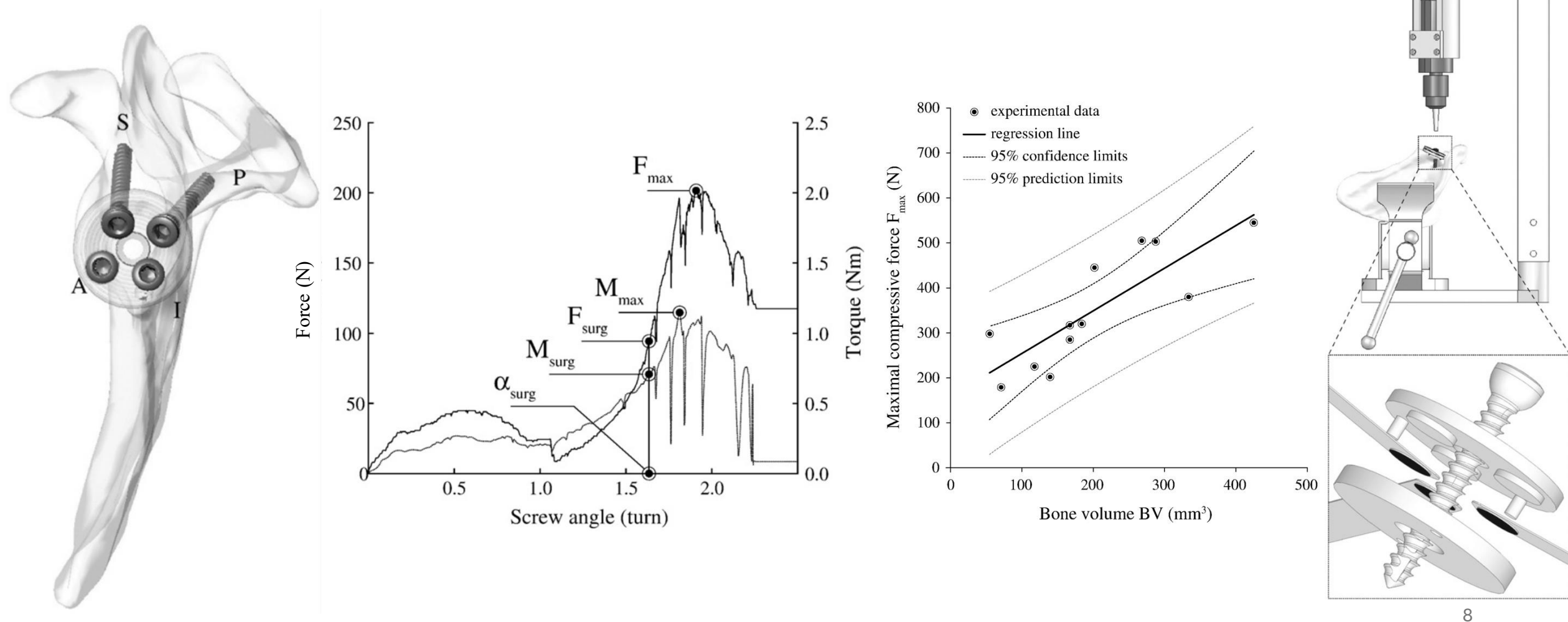
Clinical trial example

Is preoperative glenoid bone mineral density associated with aseptic glenoid implant loosening in anatomic total shoulder arthroplasty?



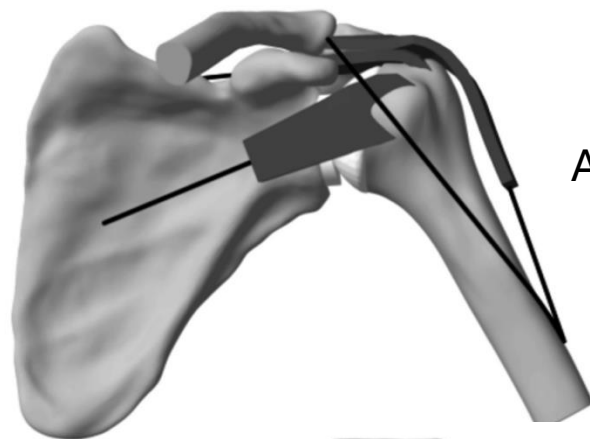
Cadaveric experiment example

Tightening force and torque of nonlocking screws in a reverse shoulder prosthesis

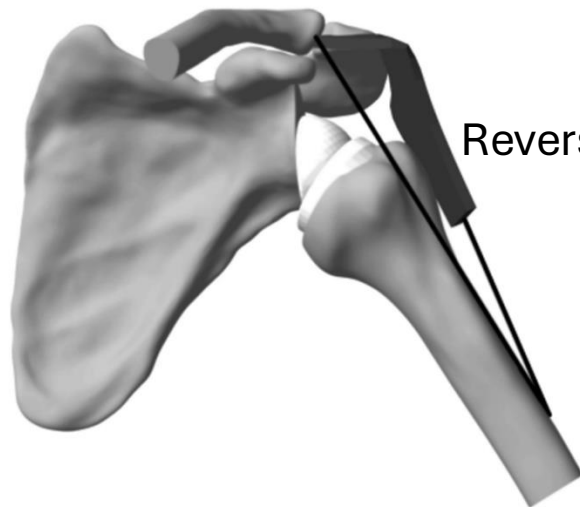


Numerical model example

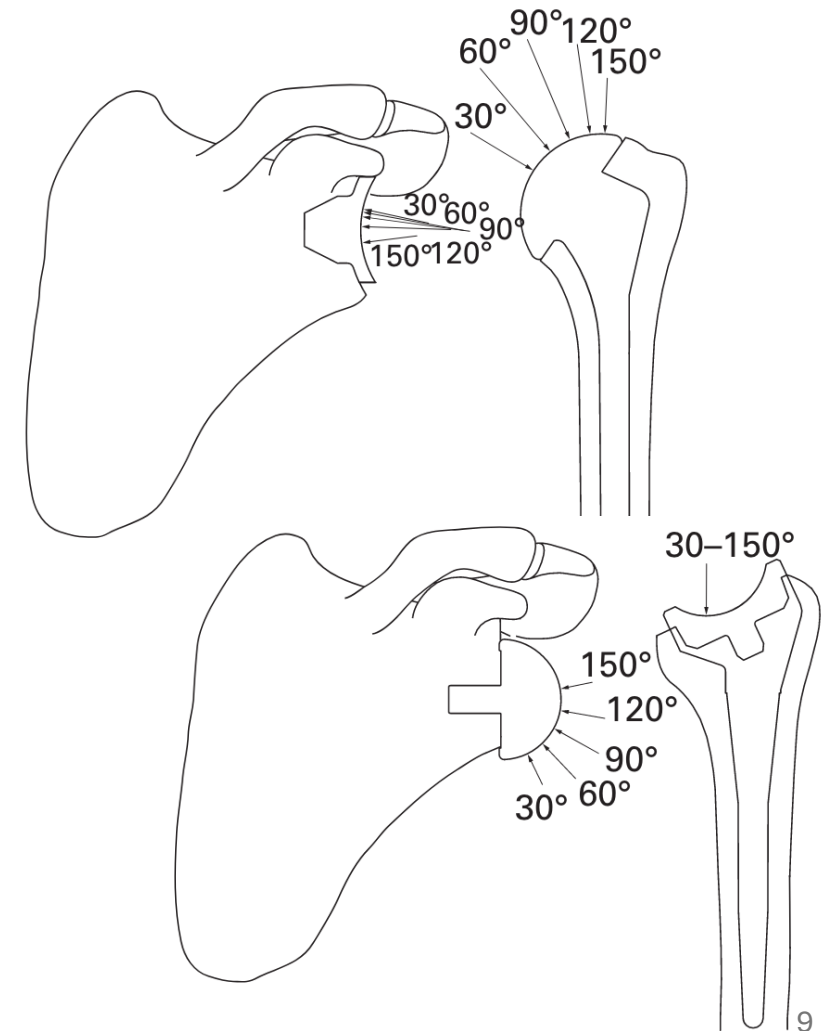
Simulated joint and muscle forces in reversed and anatomic shoulder prostheses



Anatomic Total Shoulder Arthroplasty
(ATSA)



Reverse Total Shoulder Arthroplasty
(RTSA)



Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions (2023)

Refer to
Section VI.A.(1)

Step 1: State question of interest

Example (abridged): Is the device family resistant to fatigue fracture under anticipated worst-case radial loading conditions?

Step 2: State context of use (COU):

Example: Finite element analysis will be performed to identify worst-case device sizes for fatigue fracture. These devices will then be tested on the bench.

Refer to
Section VI.A.(2)

Refer to
Section VI.A.(3)

Step 3: Assess model risk:

1. Decision consequence: e.g., the severity of possible harm is ... , probability of occurrence is ... , so overall decision consequence is ...
2. Model influence: e.g., model results will be a major but not only source of information in making the decision, so model influence is ...

Overall risk: choose from e.g., low to high

Refer to
Section VI.B

Step 4: Identify credibility evidence to be collected:

e.g.

Code verification results (Cat. 1): testing to confirm that numerical algorithms and associated code have been correctly implemented without errors

Model calibration results (Cat. 2): results showing that the constitutive model output matches experimental stress-strain measurements when material parameters are calibrated accordingly.

Bench test validation results (Cat. 3): comparison of model results with experimental measurements of force-displacement on the bench.

Calculation verification results using COU simulations (Cat. 8): mesh convergence analysis using the final COU simulations

Step 5: State credibility factors:

- Software quality assurance
- Numerical code verification (NCV)
- Goodness of fit*
- Quality of experimental data*
- Relevance of calibration results to COU*
- ...
- Model form
- Model inputs
- Test samples
- Test conditions
- Equivalency of inputs
- ...
- Discretization error
- Numerical solver error
- Use error

Step 5 (continued): State gradations and select credibility goals:

- (a) NCV not performed.
- (b) Solution compared to a solution from another verified code.
- (c) Discretization error quantified by comparison to an exact solution
- (d) Observed order of accuracy quantified and compared to the theoretical order of accuracy.

Selected Credibility Goal (based on assessed model risk): level ...

Plan for achieving Credibility Goal: ...

Refer to
Section
VI.C

Refer to
Section VI.D

Step 6: Perform prospective adequacy assessment

Rationale for why the planned evidence will be sufficient to support using the model for the COU given the risk assessment.

Refer to
Appendix 2

Optional: Submit pre-submission to receive FDA feedback on proposed plan.

Rationale
sufficient?

NO

See Section V
for options

YES

Step 7: Generate credibility evidence by executing proposed study(ies) and/or analyzing previously generated data

Results and analysis for studies listed above.

Refer to
Section VI.D

Step 8: Perform post-study adequacy assessment

Rationale for why all the evidence collected supports using the model for the COU given the risk assessment.

Rationale
sufficient?

YES

Step 9: Prepare final Credibility Assessment Report

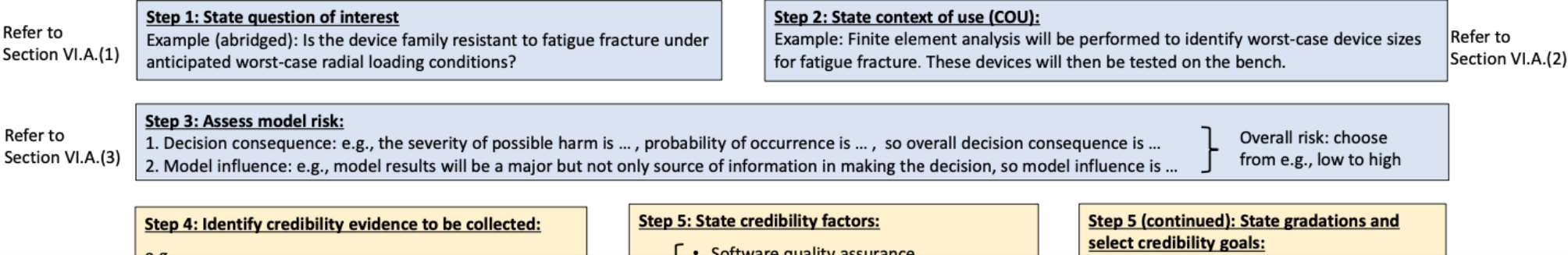
Report using the recommended structure, summarizing results of previous steps, to be included in the regulatory submission.

Refer to
Appendix 2

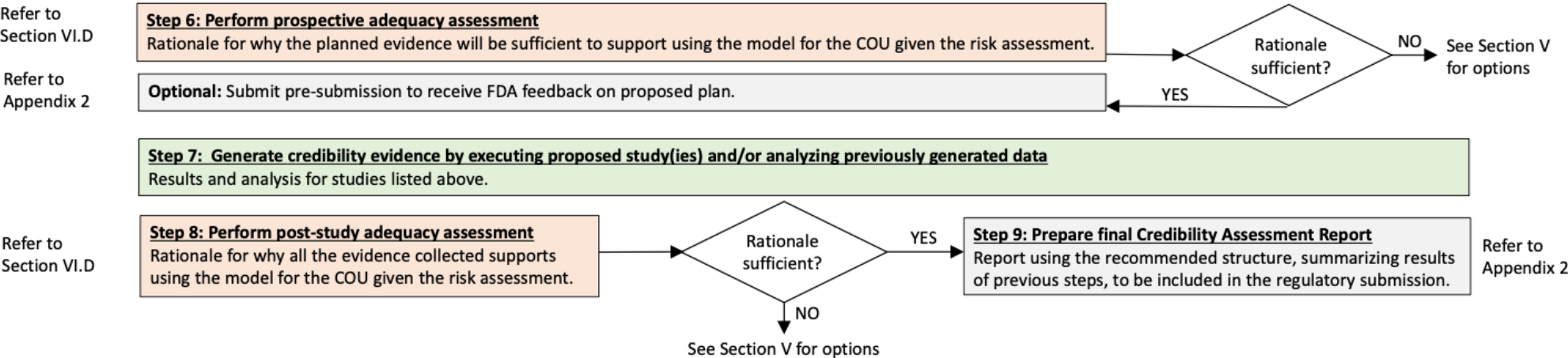
NO

See Section V for options

Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions (2023)



The FDA promotes the use of in silico clinical trials using Computational Modeling and Simulation (CM&S), in which a device is tested on a cohort of virtual patients, which is anticipated to replace or supplement clinical trials.



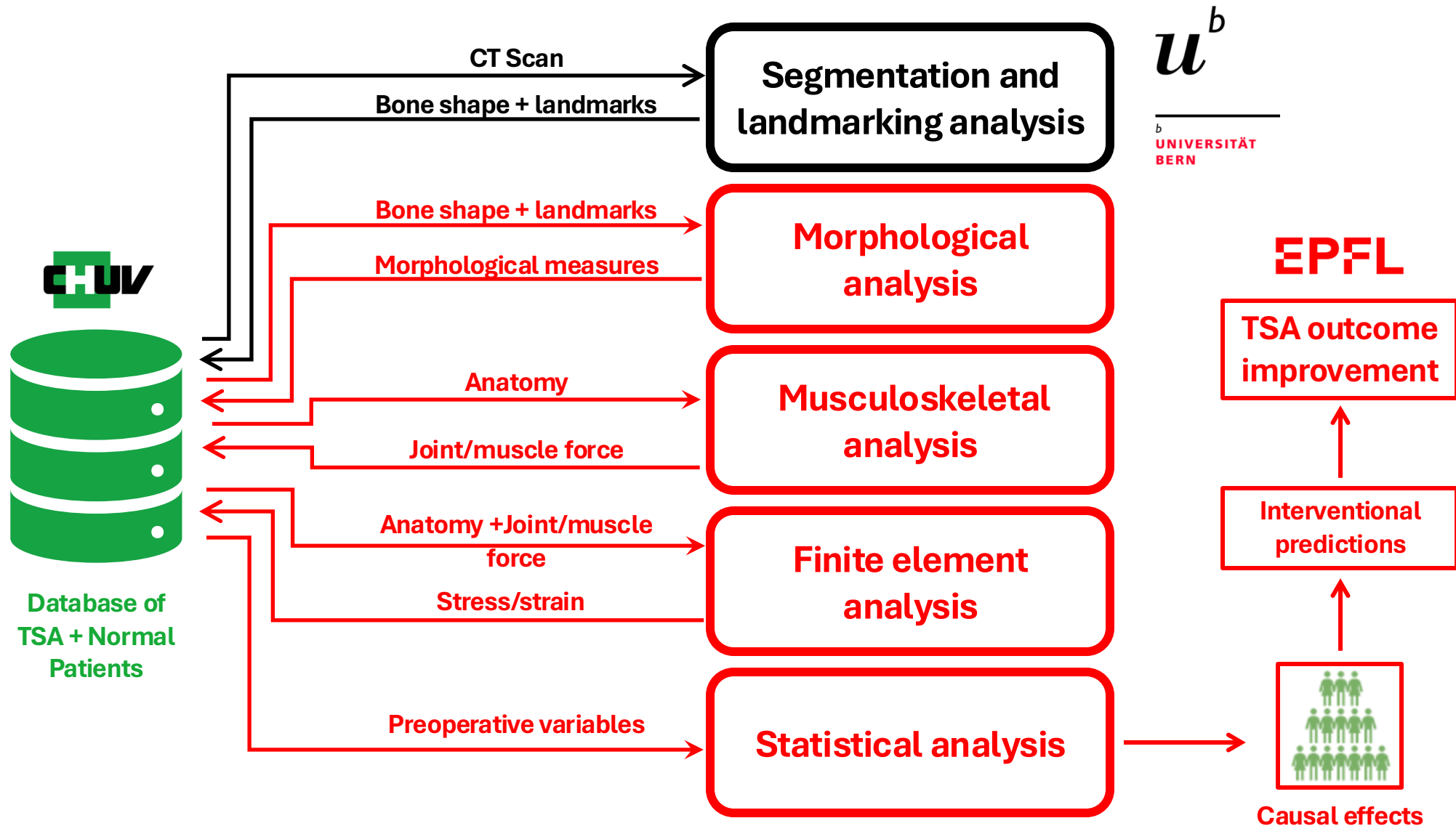
Comments on FDA recommendations

- Risk analysis
 - Uncertainty of simulation predictions
 - Potential adverse effect of false prediction
- Virtual vs real patients
 - Link with real outcome (for virtual patients)
- Link between simulated quantities and clinical quantities

Computational modeling

- Importance of Finite Element Modeling (FEM)
 - Create FEM from cadaveric data (one or few cases)
 - Create FEM from patient data (one or few cases)
 - Create FEM from (many) virtual/real patients
-
- Difficulty in automating the process for a large number of patients
 - Importance of statistical methods
 - Manage patient variability

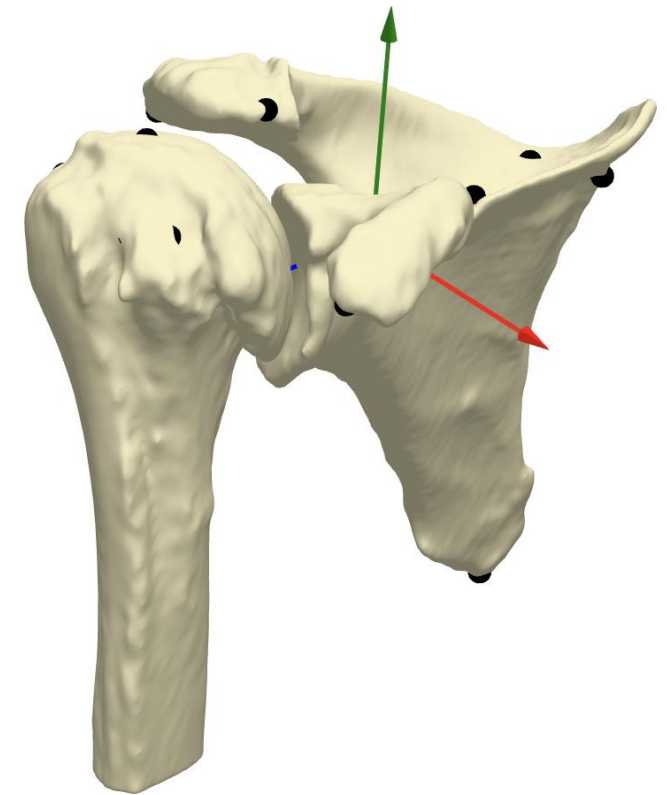
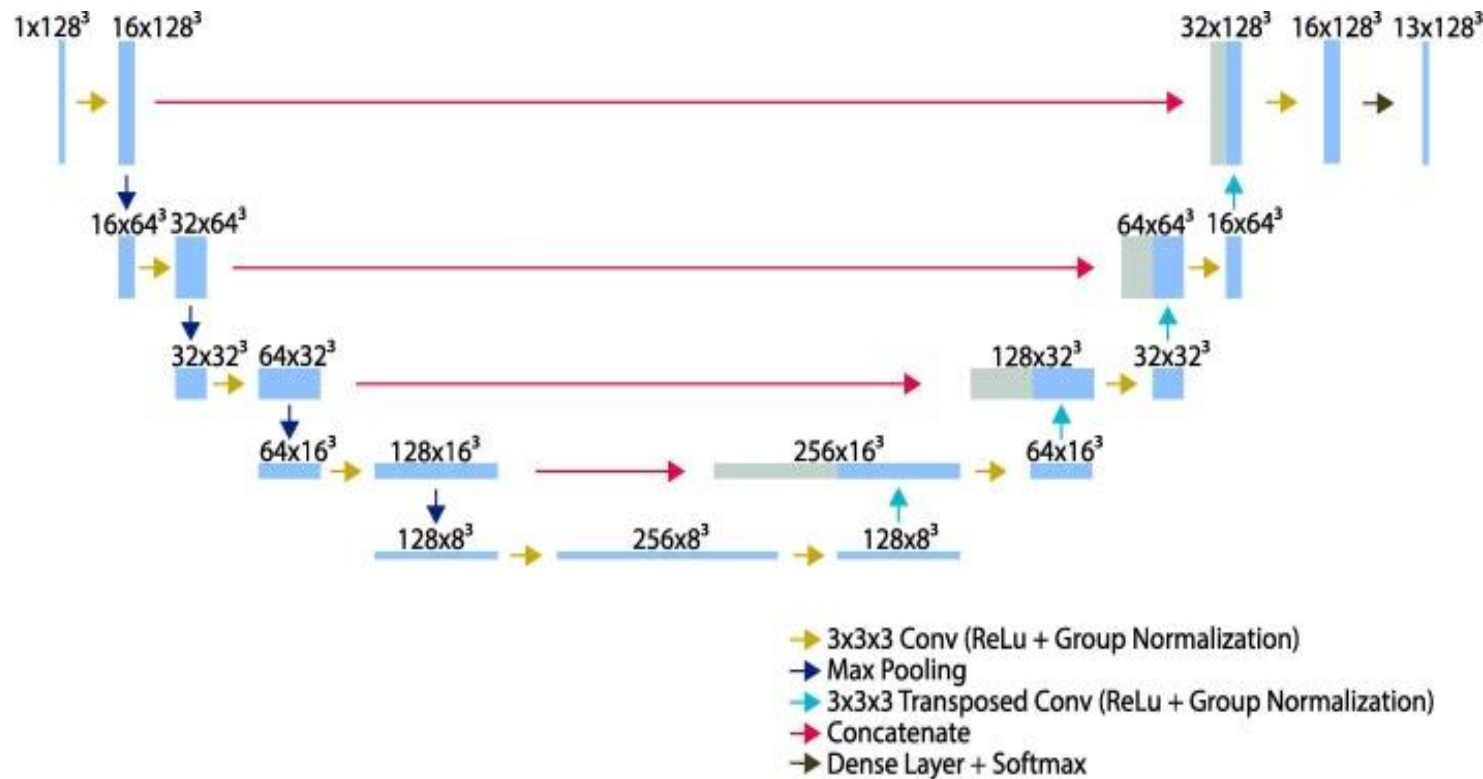
Project: Effect of preop on TSA complications



Deep Learning Model for segmentation

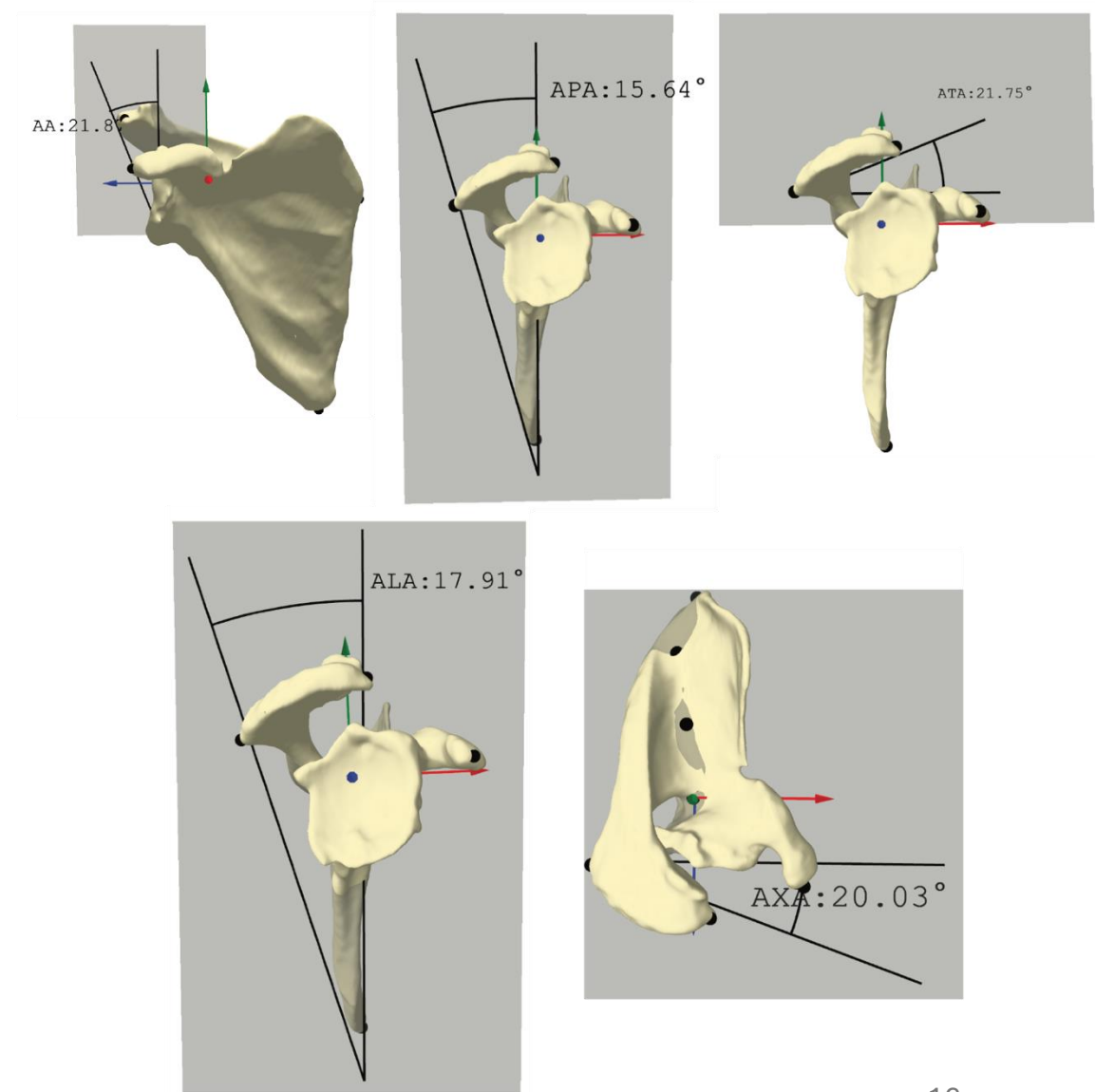
Preop CT scan → surface + anatomical landmarks of scapula + humerus

modified U-Net architecture for segmentation & landmark localizations



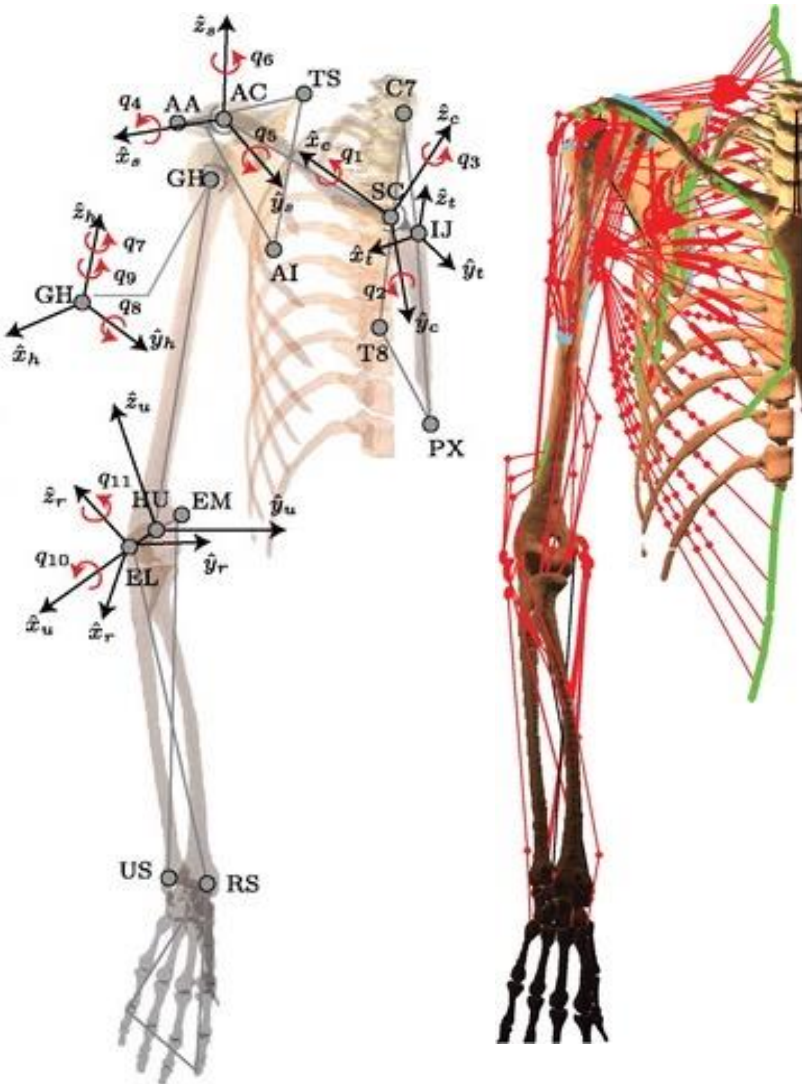
Morphological analysis

- Glenoid version angle (GVA)
- Glenoid inclination angle (GIA)
- Glenoid bone mineral density (BMD)
- Acromion angle (AA)
- Acromion posterior angle (APA)
- Acromion tilt angle (ATA)
- Acromion length angle (ALA)
- Acromion axial tilt angle (AXA)
- Rotator Cuff Degeneration
- Bone quality

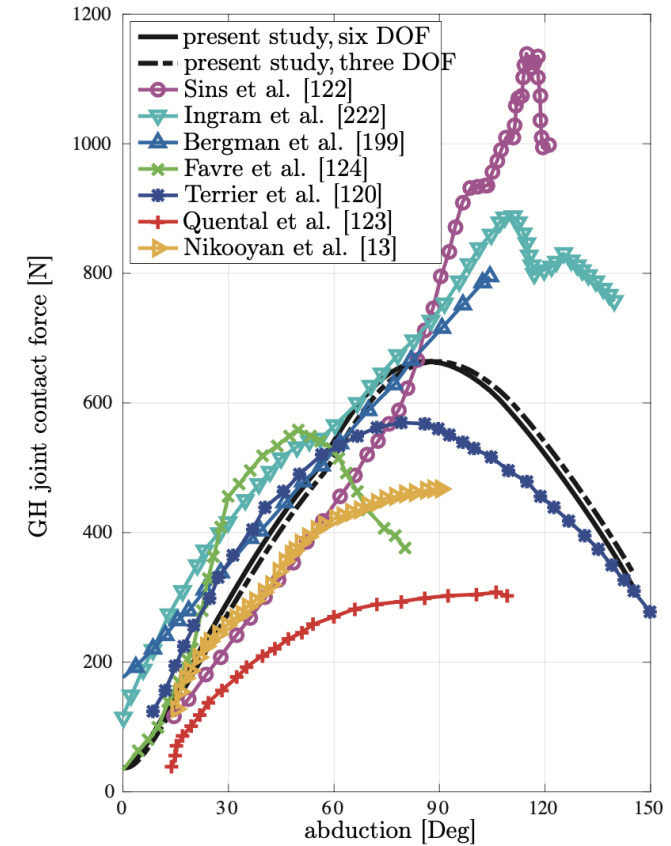


MusculoSkeletal Model

A Matlab toolbox for scaled-generic modeling of shoulder and elbow



$$\begin{aligned} \min_{\tilde{\mathbf{f}}} \quad & \tilde{\mathbf{f}}^T P \tilde{\mathbf{f}} \\ \text{s.t.} \quad & \frac{d}{dt} \left(\frac{\partial \mathcal{L}}{\partial \dot{\mathbf{q}}} \right) - \frac{\partial \mathcal{L}}{\partial \mathbf{q}} = \left[\frac{\partial \Omega}{\partial \dot{\mathbf{q}}} W \quad \frac{\Phi_{TS}}{\partial \mathbf{q}} \quad \frac{\Phi_{AI}}{\partial \mathbf{q}} \right] \tilde{\mathbf{f}} \\ & \mathbf{0} \leq \tilde{\mathbf{f}} \leq \tilde{\mathbf{f}}_{\max} \\ & \psi(\mathbf{q}, \dot{\mathbf{q}}, \ddot{\mathbf{q}}, \tilde{\mathbf{f}}) \leq \mathbf{0} \end{aligned}$$

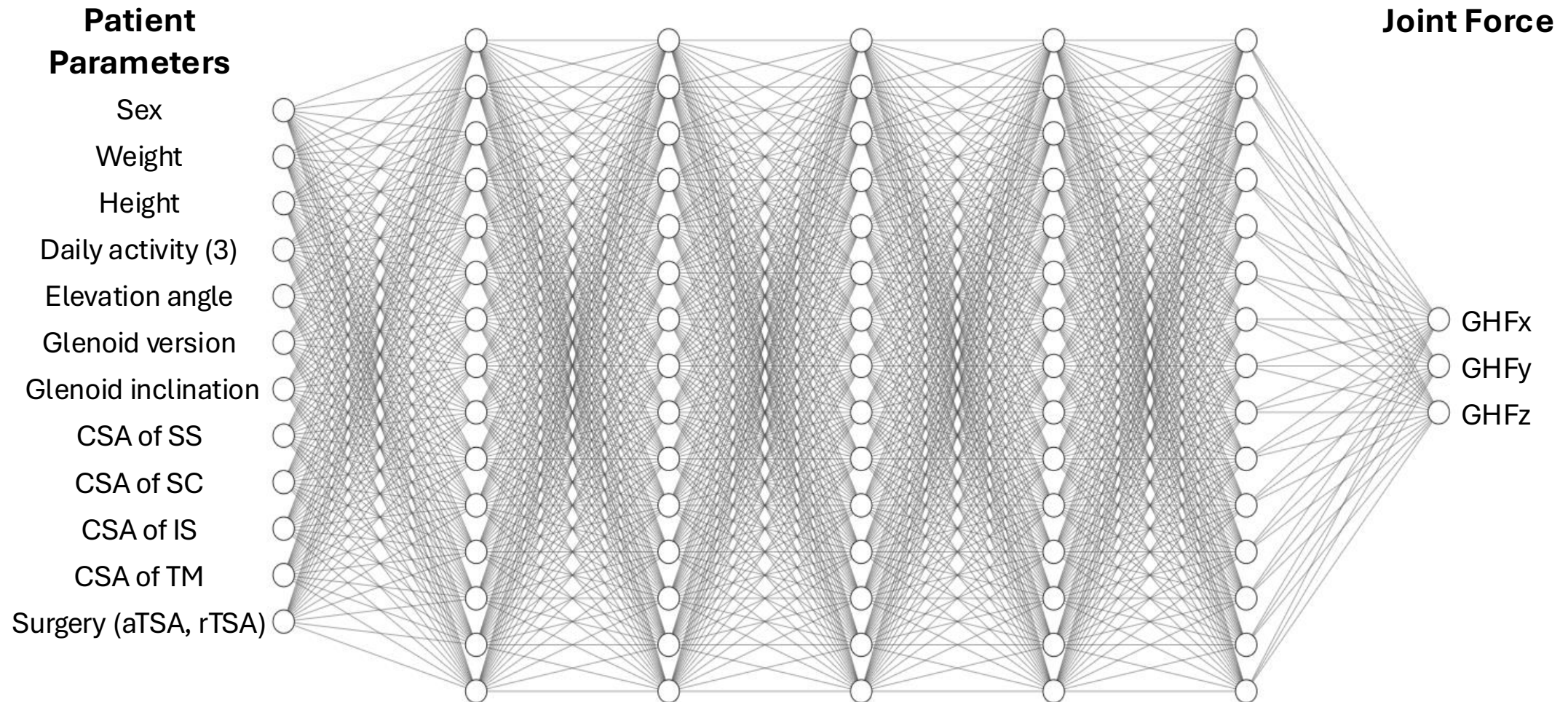


A photograph of a prosthetic arm, showing a metal upper arm and a hand assembly. The upper arm is a long, cylindrical metal tube with a flange at the top. The hand assembly is attached to the end of the tube and consists of a metal frame with a rubberized grip and a small, rectangular control unit.

[illegible]

Musculoskeletal Model → Deep Learning Model

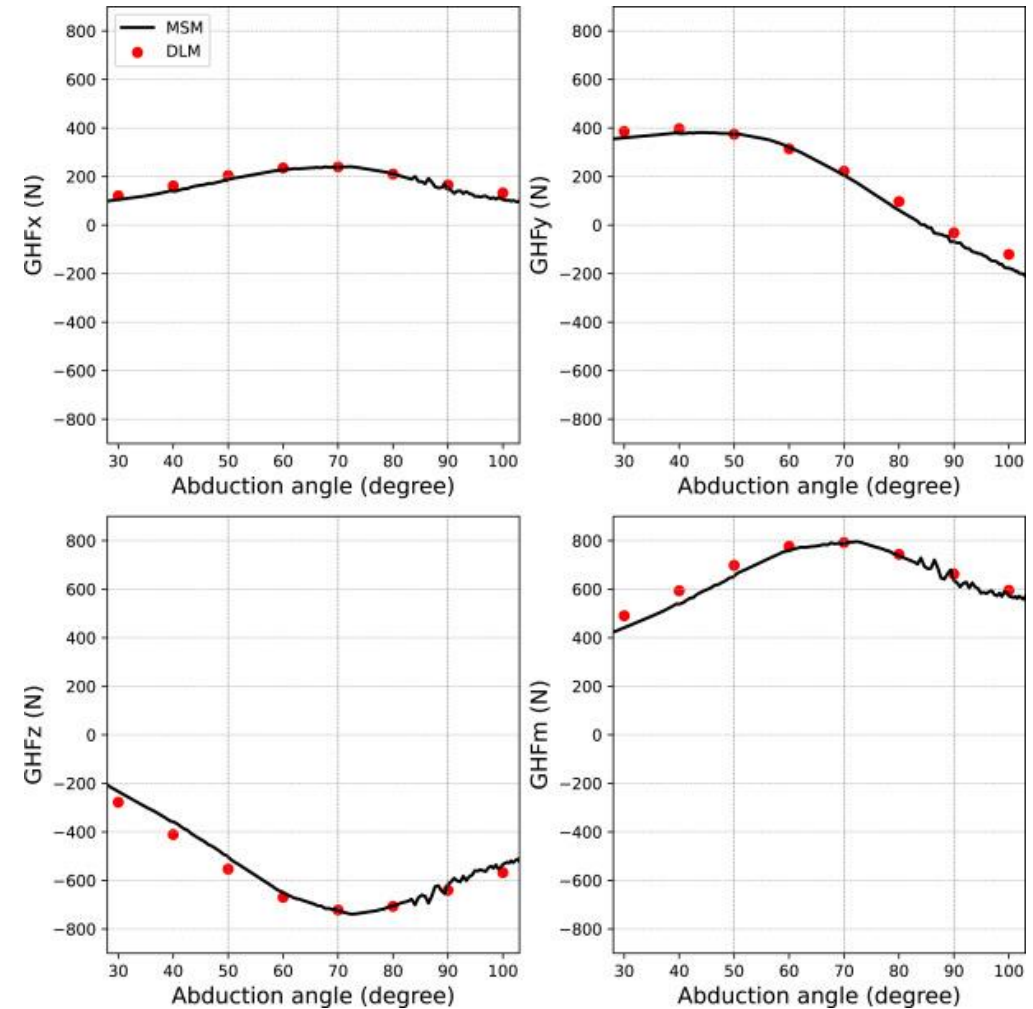
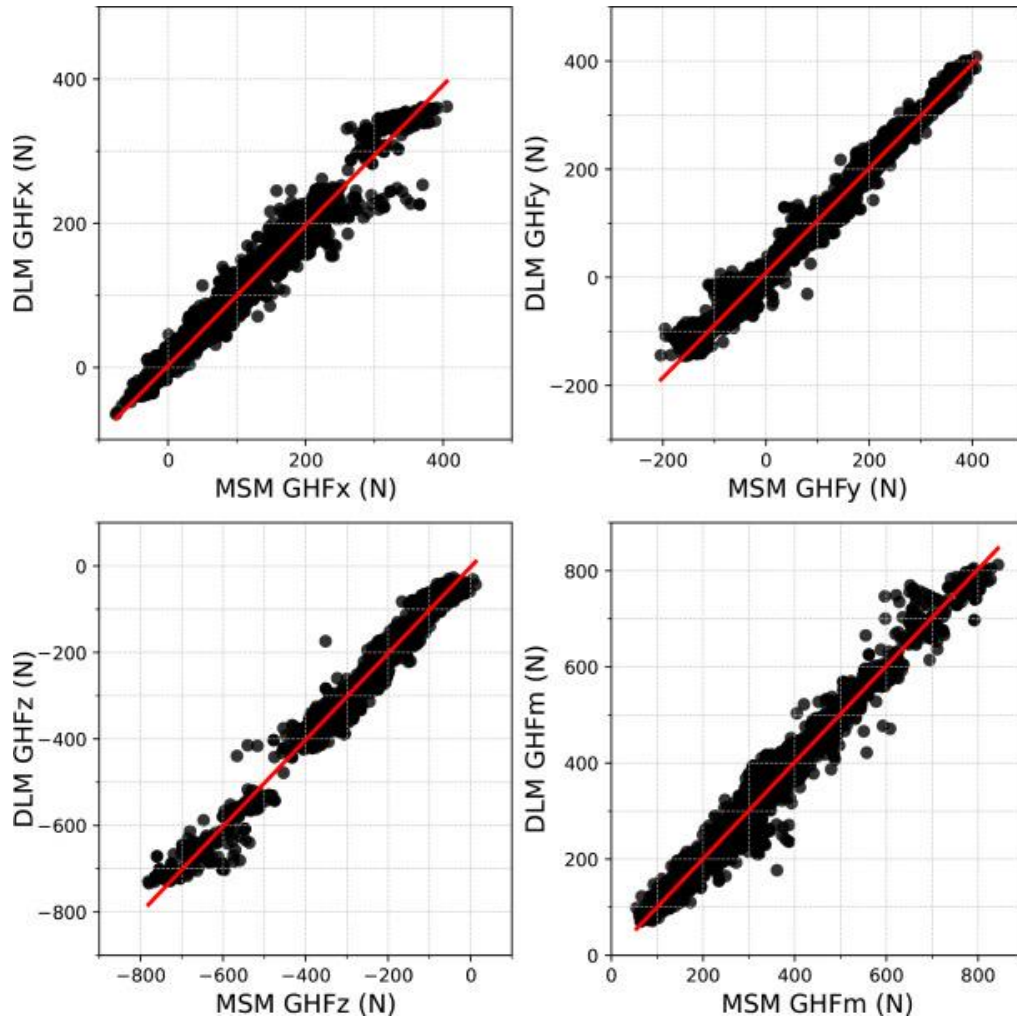
Glenohumeral joint force prediction with deep learning



Musculoskeletal Model → Deep Learning Model

- 959 virtual subjects
 - Sampling from clinical registry with Markov-Chain-Monte-Carlo
- Training (80% of subjects)
 - Fully-connected neural network
 - Training: backpropagation algorithm, descent gradient, minimize loss function
 - Validation: hyperparameters tuning with Bayesian optimization
 - k-fold validation (k=5 → 80% training & 20% validation)
→ 7 hidden layers of 250, 20, 250, 160, 90, 90, 100 neurons
 - Monte-Carlo drop-out (to avoid overfitting)
- Testing (20% of subjects, unseen by training)
 - Evaluating model efficiency

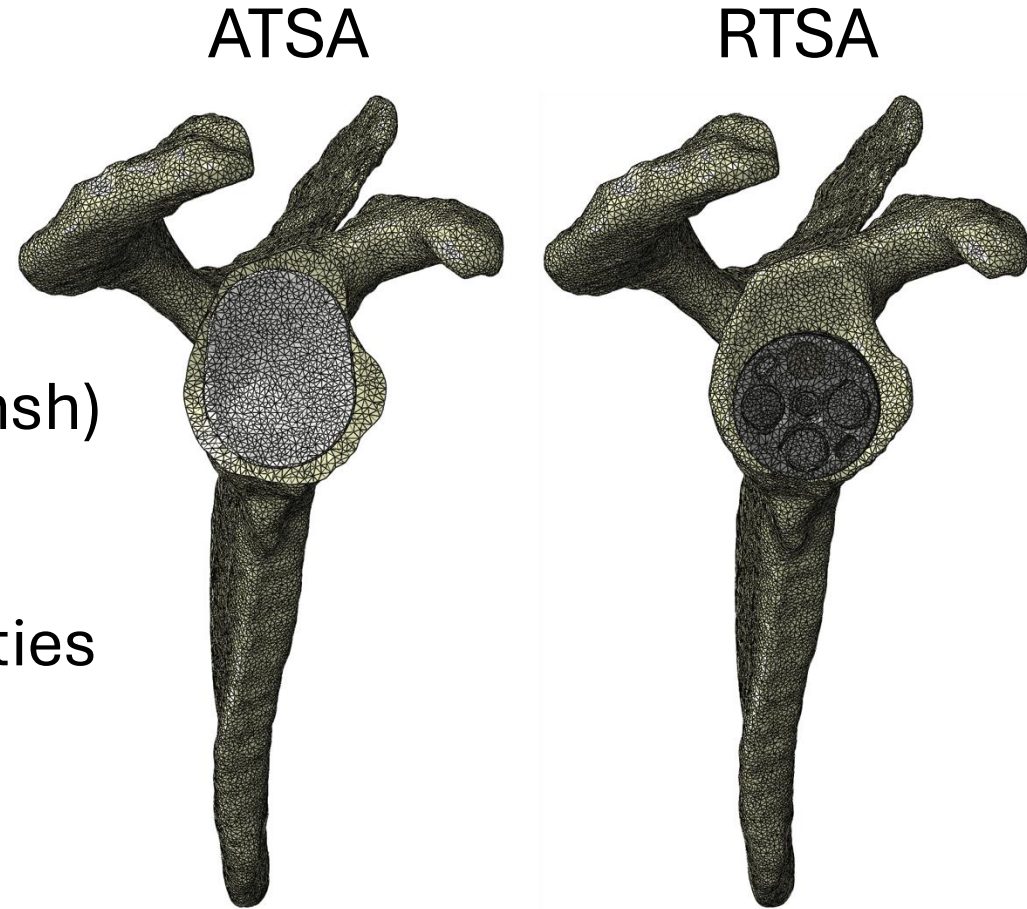
Musculoskeletal Model → Deep Learning Model



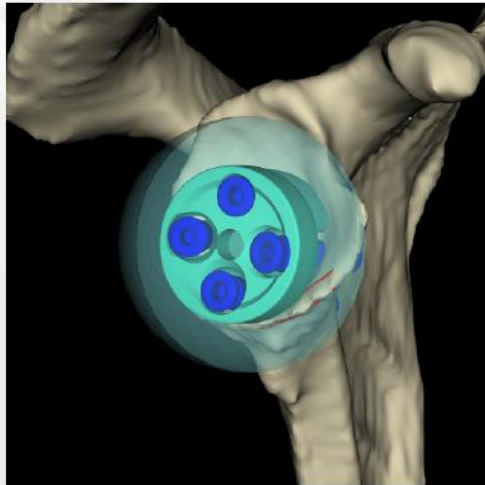
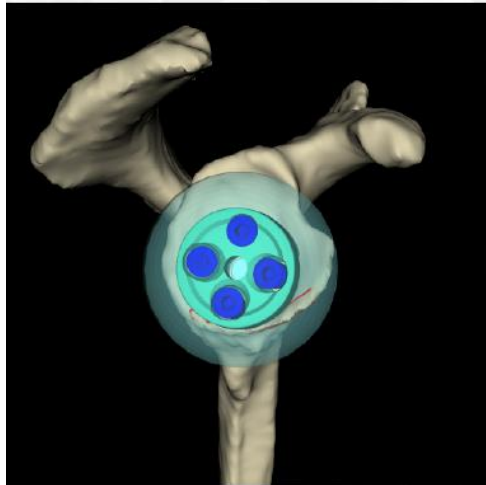
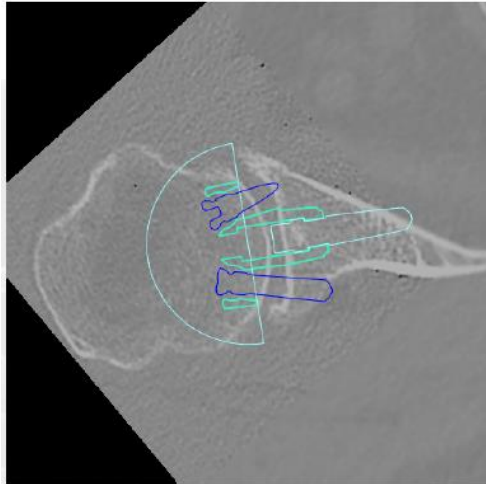
GHFm: Mean Absolute Error = 18.5 N, $R^2 = 0.97$

Automated Finite Element Model

- Bone geometry from DL segmentation
- Implant selection and positioning
(From preoperative planning)
- Scapula and implant tetrahedral mesh (Gmsh)
- Bone reaming (PyMesh)
- Bone inhomogeneous linear elastic properties
from preoperative CT (Python code)
- Force from DL MSM

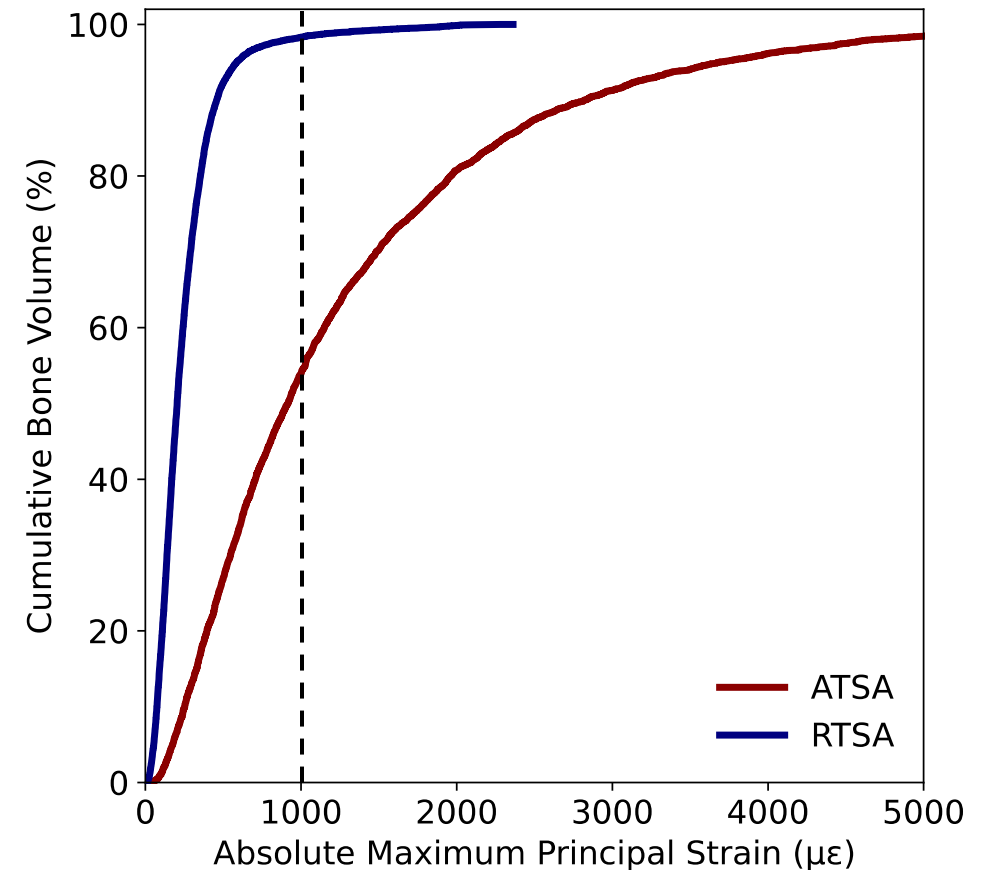
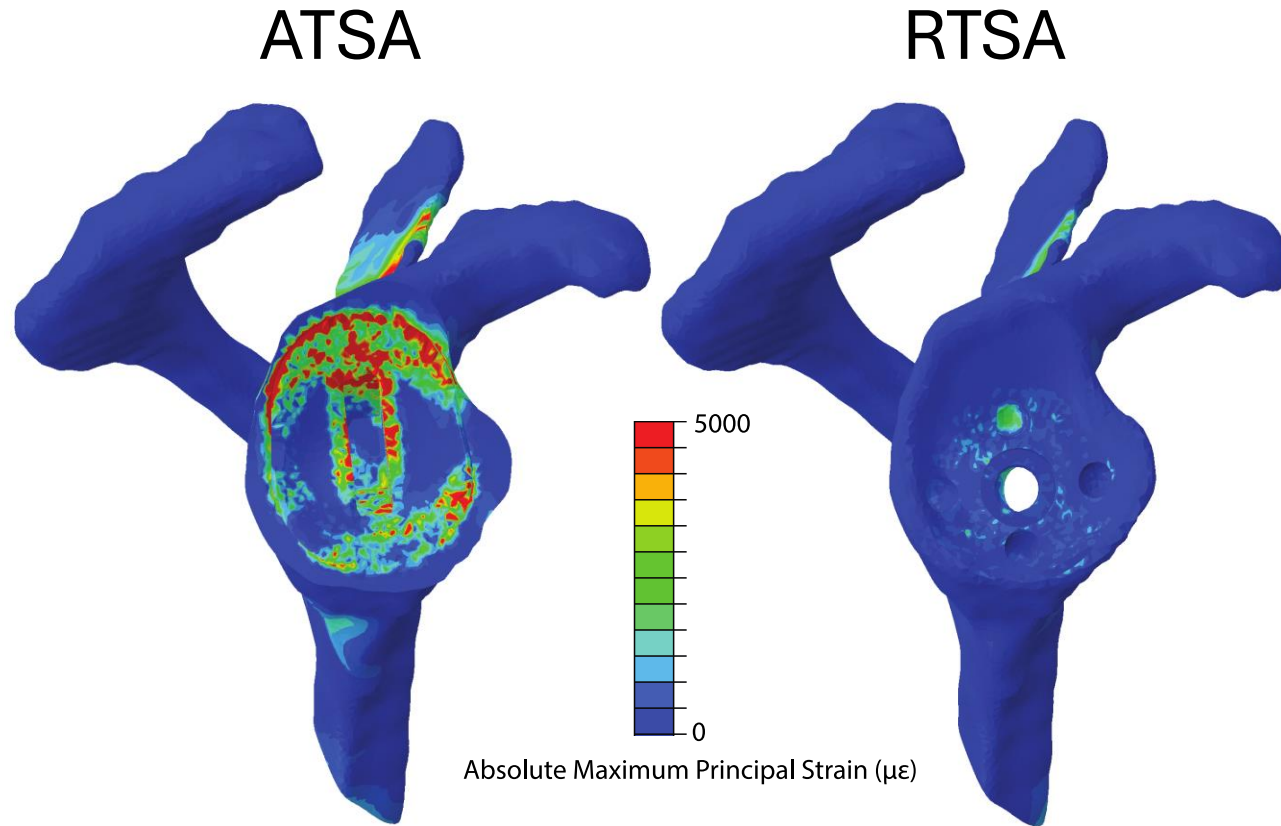


Preoperative planning



```
GlenoidImplant_PartNumber;DWJ505;;DWJ505
GlenoidImplant_PerformReversedPerforation;0;;0
GlenoidImplant_PerformReversedBasePlate;Wedge;Type de platine;Wedge
GlenoidImplant_PerformReversedBasePlateIsStandard;0;;0
GlenoidImplant_PerformReversedDiameter;25;Diamètre de la platine;25 mm
GlenoidImplant_PerformReversedOffset;0;Offset de la platine;0 mm
GlenoidImplant_PerformReversedAngle;Full;Angle de la platine;Full
GlenoidImplant_PerformReversedFixation;Central Screw;Fixation;Vis centrale
GlenoidImplant_PerformReversedFixationIsCentralPost;0;;0
GlenoidImplant_PerformReversedScrewDiameter;6.5;Diamètre de vis;6.5 mm
GlenoidImplant_PerformReversedScrewLength;30;Longueur de vis;30 mm
GlenoidImplant_PerformReversedCentralScrewPartNumber;DWJ530;;DWJ530
GlenoidImplant_Depth;-1;Médialisation;1 mm
GlenoidImplant_Inclination;4;Inclinaison glénoïdienne sup;4°
GlenoidImplant_Version;-9;Rétroversion glénoïdienne;9°
GlenoidImplant_EntryPoint;(66.590668, 92.804176, 129.965637);;(66.590668, 92.804176, 129.965637)
GlenoidImplant_DrillPoint;(66.590668, 92.804176, 129.965637);;(66.590668, 92.804176, 129.965637)
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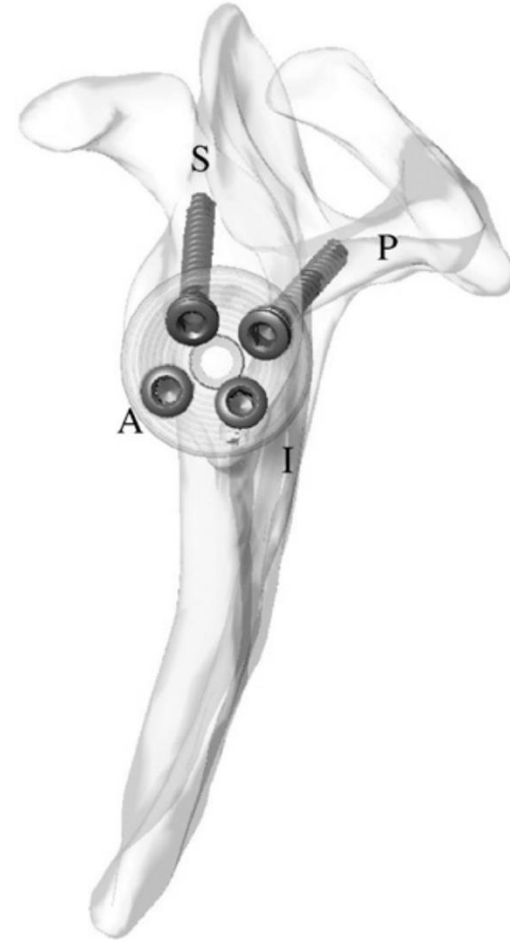
Automated Finite Element Model



Volume Of Interest (VOI): 10 mm around the prosthesis

Effect of screws in baseplate stability

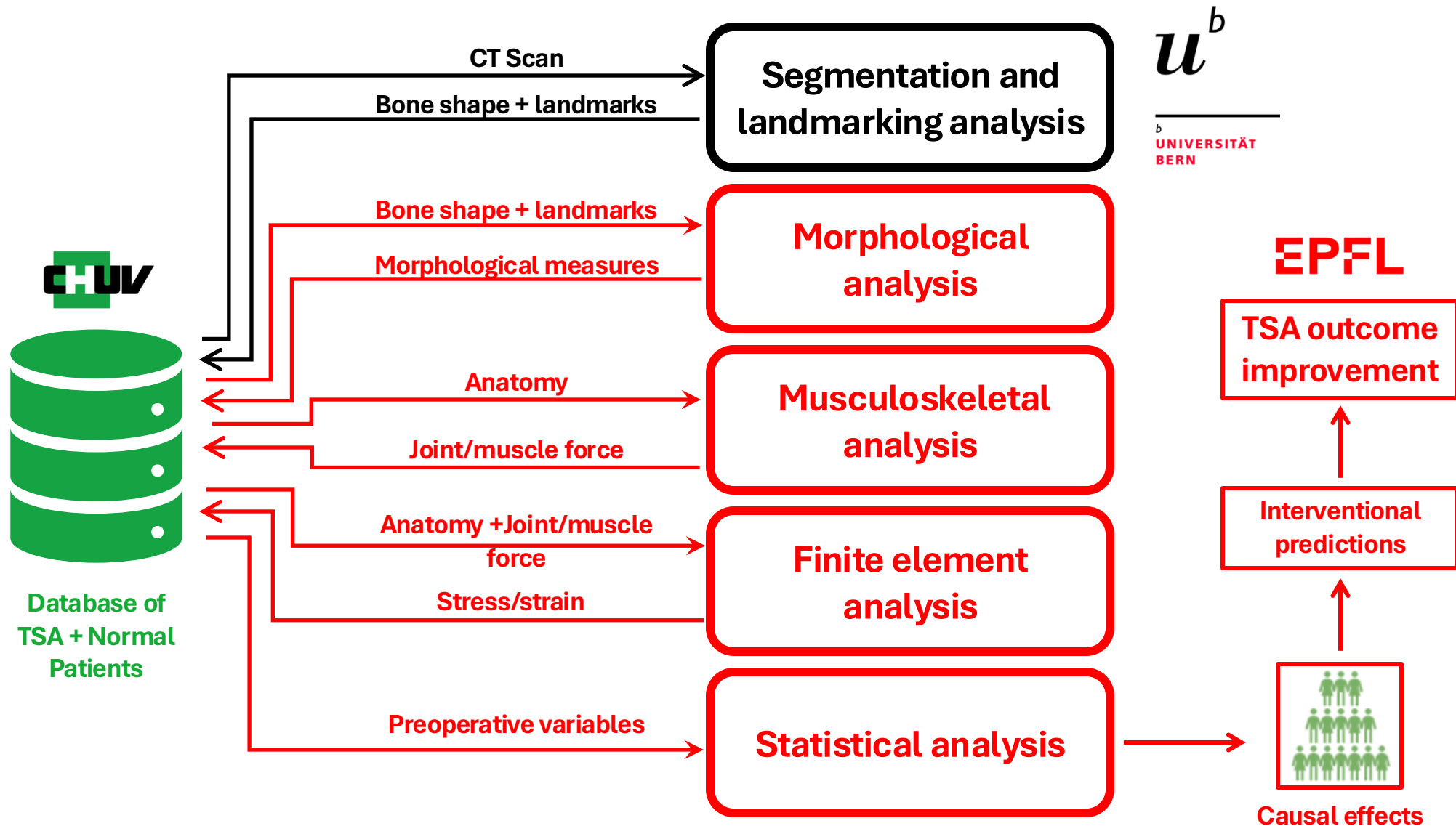
- 4 (standard) vs 2 screws (inf & sup)
- 10 patients (5 females, 56-87 years) planned for RTSA
- Joint force at 60 degrees of abduction
- Bone volume exceeding 1000 $\mu\epsilon$ (BVACS)
- Difference in %BVACS between 4 & 2 screw < 1%
- Results suggest safe to only use the sup. & inf. screws



Automation

- Entire process controlled by Python workflow
 - CT, patient clinical data (sex, age, weight)
 - Deep-Learning Model → Bone and muscle anatomy, quality
 - Musculoskeletal model → Muscle and joint force
 - FE → Bone strain
 - Merge the clinical and biomechanical data of patients

Project: Effect of preop on TSA complications



Statistics

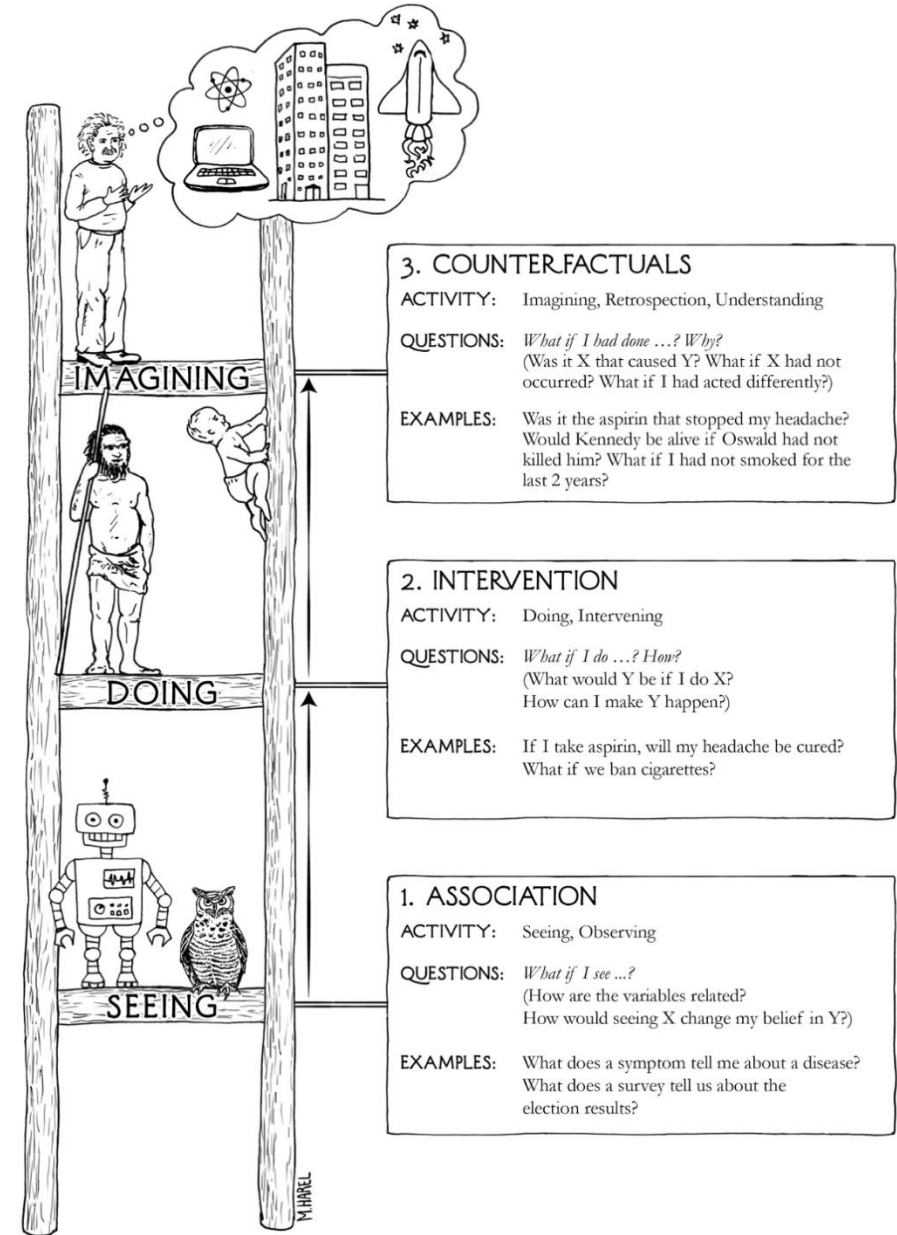
- Why?
 - Accounting for patient variability
- Association inference
 - Correlation between bone morphology/quality and mechanical strength
 - Problem of confounding variables in correctly estimating an effect
 - Both cause and effect variables dependent on a third confounding variable
- Causal inference
 - Is aging causing bone strength to decrease?
 - “Association is not causation”
 - Counterfactual “what if” questions

JUDEA PEARL
WINNER OF THE TURING AWARD
AND DANA MACKENZIE

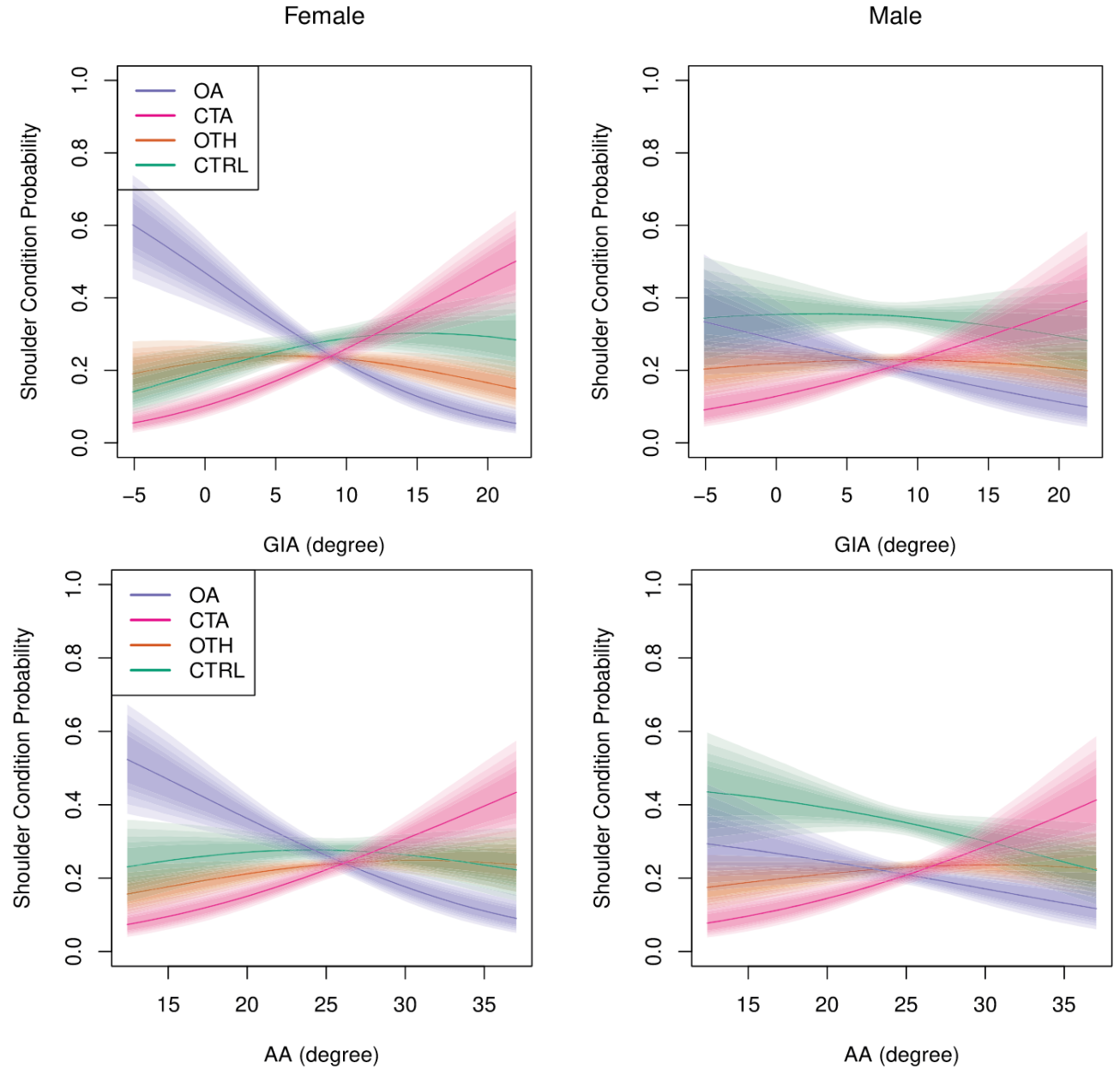
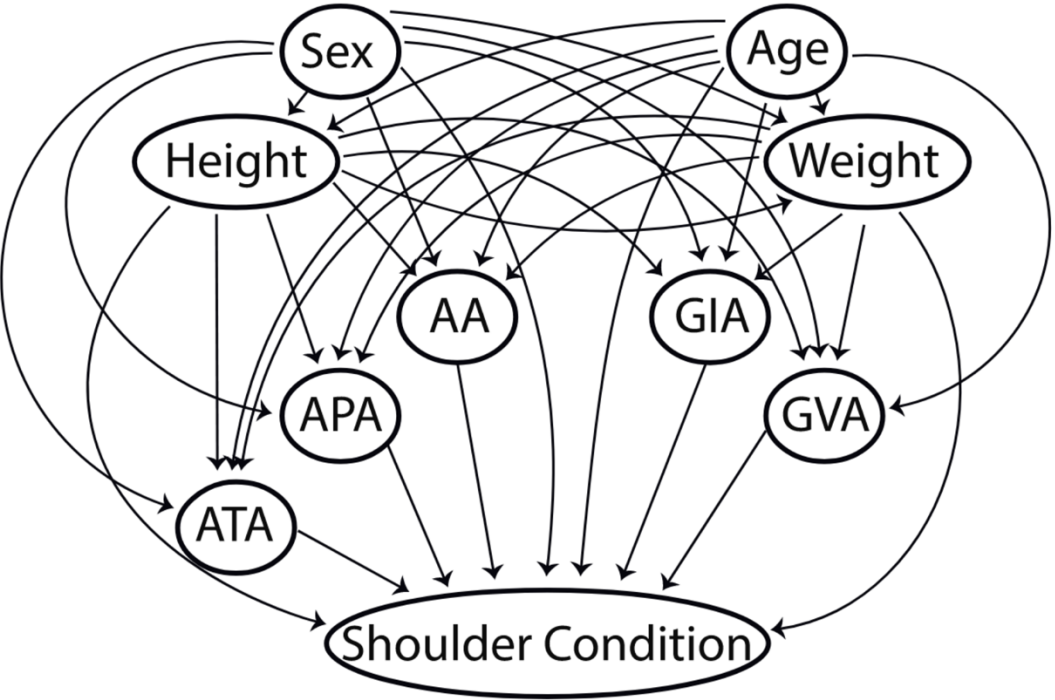
THE BOOK OF WHY



THE NEW SCIENCE
OF CAUSE AND EFFECT



Causal associations between scapular morphology and shoulder condition estimated with Bayesian statistics



Conclusion

- Computer modeling and simulation for in silico clinical trials
- Engineering background
- Link with clinical world (Surgeon, Patient, Ethics,...)
- Question-driven research
- Critical thinking