Does Your Virtual Liver Feel Like Concrete?

(Mostly) In Vivo Techniques for Measuring Soft Tissue Properties

> Mark P. Ottensmeyer, Ph.D. Simulation Group, CIMIT, MGH

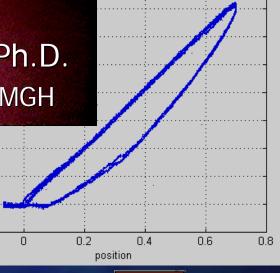
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MGH

MASSACHUSETTS GENERAL HOSPITAL







IPAM mini-review

- Satava
 - sims good enough to allow mistakes
 - digital libraries of patient specific cases (from Virtopsy)
- Teran/Oliker/Cutting
 - fast FE, spring-mass models for plastic surgery
 - deformation & cutting
- Terzopoulos
 - facial tissues, neck/body muscles
- Schill
 - ophthalmic surg sim deformation & tearing
- Meglan
 - generalizability, "provenance"
 - Top-down face validity requires redo for each new sim
- Soft tissue model material parameters how do you get them?

Tissue properties - a black hole Satava, c. 2001

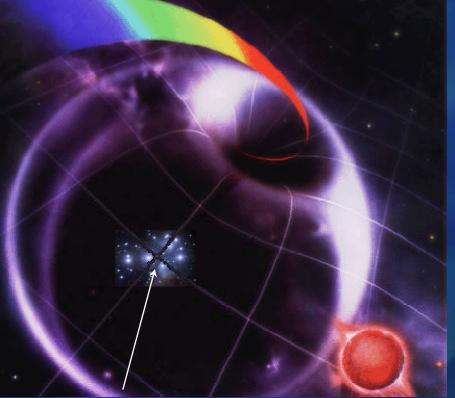
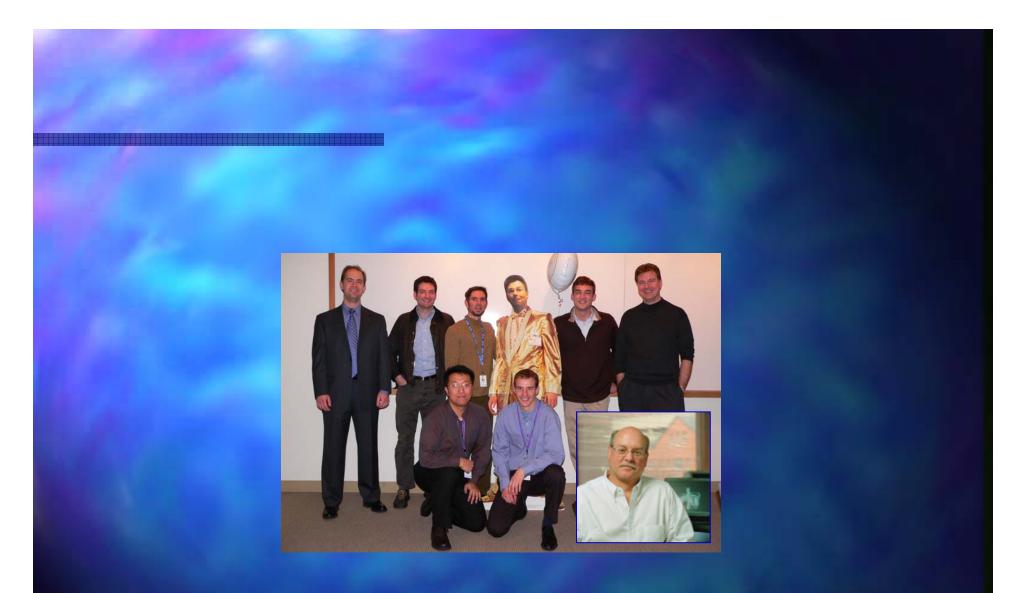


image: National Geographic Picture Atlas of Our Universe, 2nd ed., 1986

c. 2008: Harders, De, Ottensmeyer & friends!

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basic science and proof-of-concept systems for medical training through simulation

Multi-disciplinary research team

M.D. (radiology), mech. eng., comp.sci., industrial designer, fine arts



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Scientific Computing Applications in Surgical Simulation of Soft Tissues

COMETS

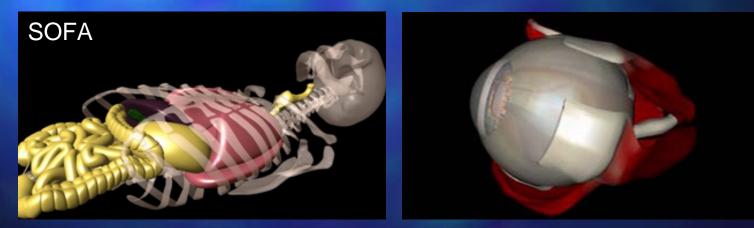




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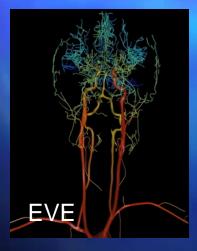


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Student practices smallpox inoculation on SITU



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Outline

in vivo tissue testing techniques & devices

- taxonomy axes?
- compliance testers
- elastographic techniques
- briefly cutting/piercing
- applications sprinkled in
- summary & a few extra slides

Possible tissue testing taxonomies

- Measurement interaction technique
 - Tension, compression, indentation, shear, aspiration
 - Puncture, cutting (single blade/scissors), crushing, fracture
 - Non-contact, non-invasive
- Rate/range of interaction
 - Static/quasi-static (ignoring viscosity)
 - Manual manipulation rates (2Hz or less)
 - Soft impact, moderate frequency (<300Hz)*</p>
 - High speed impact, ultrasound response
 - Strain level: linear to non-linear material and geometric domain

Tissue type

- Solid organ (liver, kidney, brain, muscle...)
- Hollow organ (intestine, stomach, bladder, vessels...)
- Structural (bone, cartilage, tendon, ligament...)
- Others?

Application

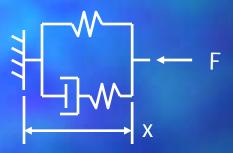
- Surgical simulation (real-time & JND constraints)
- Tissue engineering, implants, prosthetics (offline models?)
- Physiology simulation (voice production here's the *)
- Body armor development (model impactor + armor + underlying tissue)

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Living Tissues

Material properties/behaviors

visco-elasticity—standard linear (Kelvin) model



- Prefer geom.-indep. properties, *not* spring consts.
- Non-linear, *poro*-visco-elastic, anisotropic, inhomogeneous, age/temp/pathology-dependent
- Independent experiments for each parameter!
- Yamada ('70), Duck ('90), others: in vitro

Living Tissues

- Measurement complications
 - Invasiveness of testing—surgical access to organs
 - Motion corrupts data: cardiac, pulmonary action
 - Limited testing periods
 - Non-ideal tissue "samples": no standard shapes
 - Tensile tests difficult
 - Humidity, temp., body fluids—effects on hardware
 - Human testing protocol approval!
 -

Measurement Techniques

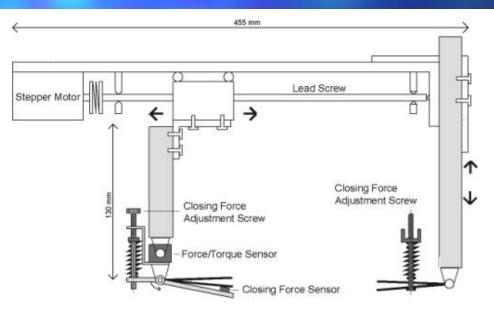
- Compliance testing
 - Deform tissue locally, measure "F(t) vs. X(t)"
 - Use simple approximation or iterative FEA to extract parameters
- Elastographic testing
 - Image strain field (2-D, 3-D), motion amplitude
 - Invert to generate qualitative elastograms
 - Iterate on inverse problem for quantitative
- Cutting & needle insertion
 - Recording F(t) vs. X(t)
 - Separate elastic, fracture, frictional components
 - Currently instrument-specific

Compliance techniques

- Deformation modes
 - tension
 - compression
 - indentation
 - side trip into bench top "life support"
 - torsion (shear)
 - aspiration/suction

Compliance: tensile testing

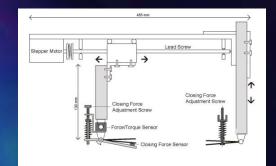
- Tendick, et al.; UCSF/Berkeley
 - GiPSi: open source framework for surgical simulation
 - Enhanced perception for soft tissue manipulation
 - Interactive-rate FEM techniques
 - Creation of tissue property "atlas"



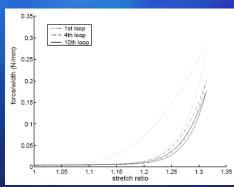
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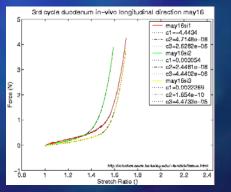
Compliance: tensile testing

- Uniaxial tensile testing apparatus
 - Babcock graspers; open abdomen



- in vivo/vitro porcine stomach, sm. bowel, gall bladder (Brower et al., MMVR01)
- 40Hz control/sampling; >150mm motion; 0-6N applied
- Curve fitting
 - $F(\lambda) = \alpha e^{\beta \lambda}; \ \lambda = I/I_0$
 - Tests include response to pre-conditioning: large for in vitro
 - online resource for force-stretch ratio data



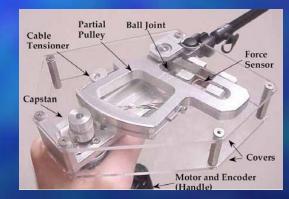


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Compliance: compression tests

- BioRobotics Lab, U. Washington
 - Hannaford, Rosen, et al.
 - Understanding surgical gestures, force/position range
 - Blue Dragon, Red Dragon, Markov model description
 - Improving tactile feedback for MIS
 - Supporting surgical simulation community







http://brl.ee.washington.edu

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Compliance: compression tests

- Motorized Endoscopic Grasper
 - Babcock grasper, MIS (10mm port), usually open laparotomy
 - in vivo porcine solid & hollow organs
 - improved haptic tissue discrimination; characterize tissue in vivo vs. post mortem
 - testing up to 3Hz; 30mm RoM; 25N (70 max) force (surgical scale)



FREG

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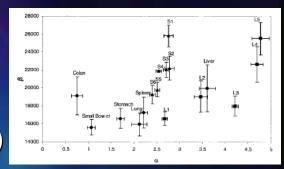
MEG

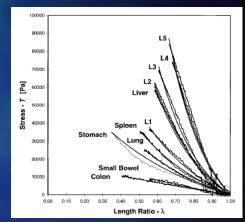
FREG/MEG: selected results

Tissue stiffness (FREG) (Rosen et al., MMVR98)

- distinguishable stiffness: *in vivo* porcine liver, spleen, small bowel, colon, stomach, lung
- Curve fitting: $\sigma(\lambda) = \beta(1-e^{\alpha(1-\lambda)}); \sigma = F/A_0; \lambda = I/I_0$
- Tissue stiffness (MEG) (Brown et al., MICCAI03)
 - liver/small bowel in vivo \Rightarrow in situ \Rightarrow ex corpus (3x)
 - preconditioning, stress relax'n effects differ post mortem, changes between vivo, ex corpus @ 25hrs
- Color change (De et al. MMVR06)
 - MEG compression, Canon Powershot A80, spectrophotometer, subjective validation
- Damage thresholds (De et al., IJRR07)
 - porcine liver (<80kPa @ 30s), ureter (~100kPa), small bowel (~100kPa)
 - H&E (morphology), MPO IHC (inflammation), caspase-3 IHC (apoptosis) staining



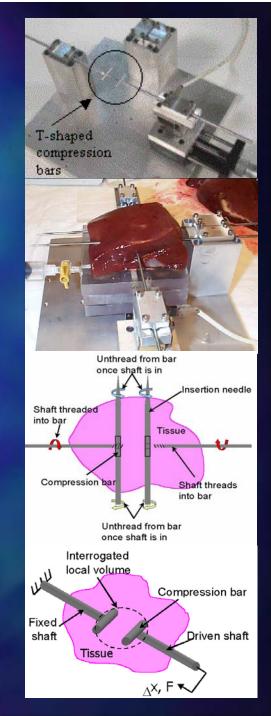






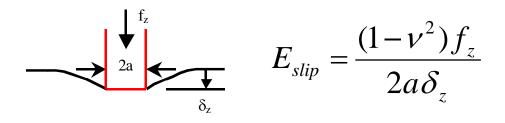
Compliance: compression tests

- BioRobotics Lab, Harvard U.
 - Howe, Kerdok, Maeno, et al.
 - "Enabling Technologies for Advanced Soft Tissue Modeling"
 - Internal parenchymal tester for solid organs
 - Motorized, integrated with NELP system
 0-100mm/s, 36% strain (7mm compression)
 - Proof of concept results (Kerdok&Howe'03)
 - QLV model, 3 time constants: 0.102, 1.47, 27.76s



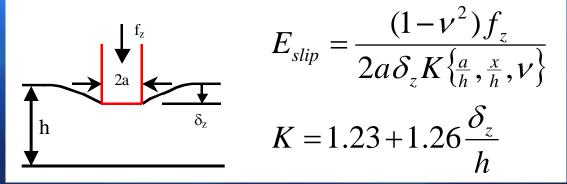
Compliance: indentation

- Closed form solutions
 - linear, isotropic, homogeneous, semi-infinite
 - normal indentation (frictionless)



Hayes' correction (Hayes et al., J.Biomechs72)

correction exists for hemispherical indenter as well



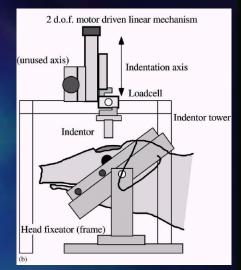
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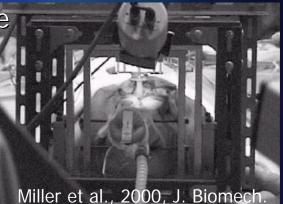
Compliance: indentation

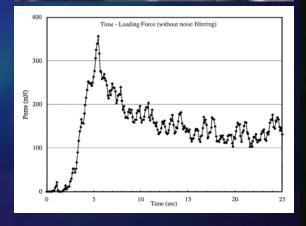
- Common method for tissue testing in vivo
 - Miller, U. Western Australia: porcine brain
 - Carter, U. Dundee, UK: human liver
 - Ottensmeyer, MIT: porcine liver
 - Kerdok, Harvard: porcine liver, spleen
 - Tendick, UCSF; Srinivasan, MIT: porcine abdominal tissues
 - De, RPI: porcine tissues, human cadavers

Compliance: indentation tests

- Intelligent Systems for Medicine Lab; U. Western Australia
 - Miller, et al.
 - non-rigid registration, neurosurgical planning & simulation, predicting injury due to baseball impact
 - porcine brain in vivo, 10mm flat cylindrical indenter
 - Imm/s max V; 3.9mm indentation used; 400mN max (applied *in vivo*)
 - Iterative FEA using hyperviscoelastic constitutive law, MRI for BCs



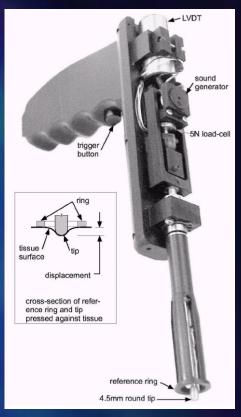


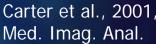


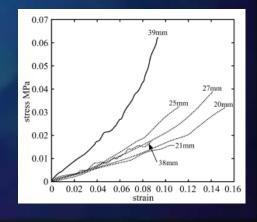
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Compliance: indentation tests

- Surgical Skills Unit, Dundee U., UK
 - Carter, Cuschieri, et al.
 - diagnostics, tool design, surgical simulation
 - manual application: 5mm (10 max) in vivo; ~1N (5 max) in vivo
 - 4.5mm hemispherical indenter, reference ring 12/18mm ID/OD
 - first human liver in vivo!
 - healthy vs. diseased (cholestatic liver w/bile obstruction: 2x stiffness)
 - porcine liver & spleen in vitro



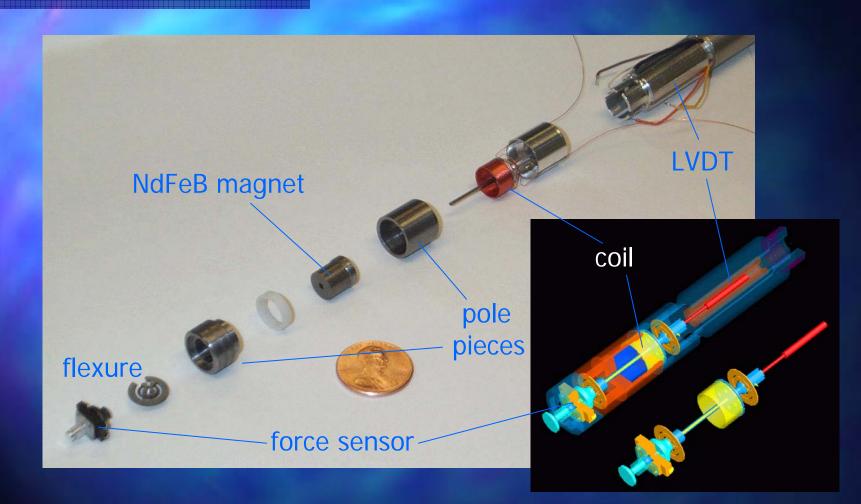




Compliance: indentation tests

- Haptics Laboratory, MIT
 - Ottensmeyer, Salisbury
 - support for planned laparoscopy simulator
 - minimally invasive; 2kHz sampling; 80Hz resonance; 1mm RoM; 300mN max force; 5mm flat cylindrical indenter, 12mm OD
 - characterization of small defm'n frequency response
 - in vivo porcine liver, spleen; various in vitro

TeMPeST detail

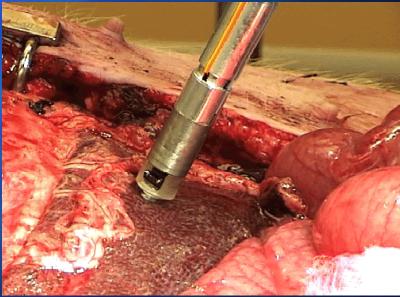


TeMPeST in vivo animal testing

Details

- ARC (Dartmouth), HCMIS
- pigs in surgical tool testing protocol
- laparoscopic & open
- video clip





TeMPeST in vivo animal testing

Typical test sequence



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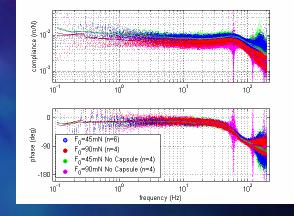
TeMPeST results

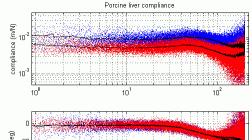
A few examples...

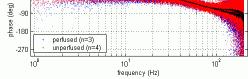
- examination of effect of capsule
 - stiffer than underlying parenchyma
- effect of organ perfusion
 - blood pressure pre-stresses capsule

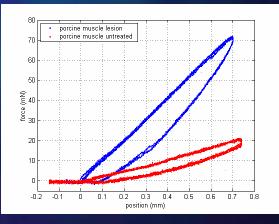
porcine muscle

quasi-static comparison of normal tissue with HIFU lesion









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A short detour...

- in vivo "gold standard" subject to limitations
 - time, cardiac/pulmonary action, etc.
- *in vitro* problems
 - coagulation, loss of fluids, change in boundary conditions

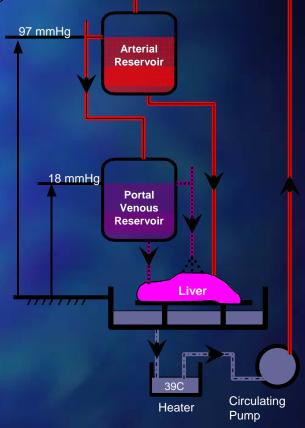
Perfusion

- inspired by transplant literature, without chilling
- in vitro "silver standard"
 - maintain blood pressure (venous, arterial)
 - maintain temperature
 - maintain osmotic, oncotic balance

Normo-thermic Liver Perfusion System

Perfusion system

- provides physiological solution to whole organ
- for liver: hepatic arterial and venous pressures, drains through portal vein
- physiologic temperature control
- hydration maintained
- Lactated Ringer's w/dextrose, Hetastarch (osmotic & oncotic balance)



Perfusion Rig

Initial version

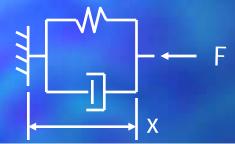
- hydrostatic supplies of perfusate: high elevation for arterial supply, lower elevation for venous
- pump, heater below bench

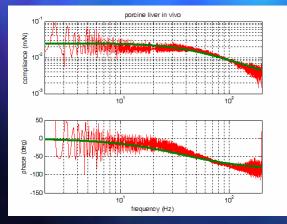


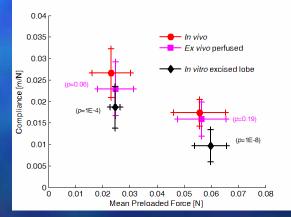
Perfusion validation

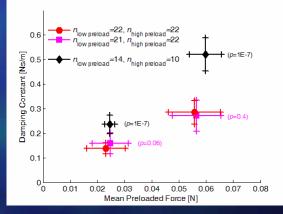
■ TeMPeST tests

- compared in vivo, perfused, unsupported conditions
- response similar to linear spring-damper
- statistical comparison of stiffness, damping coefficient





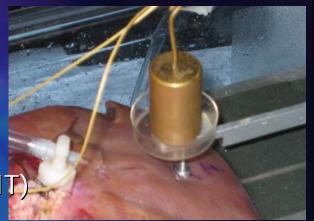




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Compliance: indentation

- BioRobotics Lab, Harvard
 - Kerdok, Howe (BRL); Ottensmeyer (CIMIT)
 - large deformation tissue characterization
 - creep characterization, testing *in vivo vs.* perfused *in vitro vs.* unperfused *in vitro*
 - 0.25" flat cylindrical indenter; 1kHz sampling; 10mm RoM; 20/100/200g step load (manually placed); open abdomen
 - porcine liver in vivo vs. in vitro
 - validated perfusion system for large deformation



Displacement potentiometer

Displacement potentiometer

Portal vein perfusion

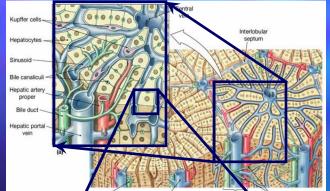


Indentor and weight cup

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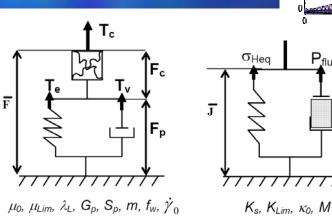
Compliance: modeling

- Improved model
 - liver anatomy suggests more complex model
 - hyperelastic, poro-viscous elements
 - Socrate/Kerdok modification of Arruda-Boyce
 - <u>motorized indenter experiments</u>

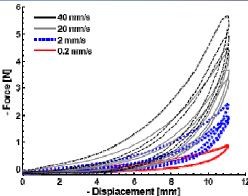


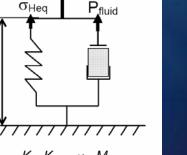








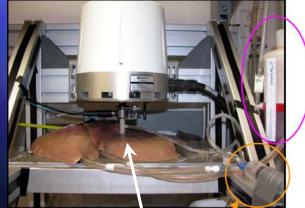






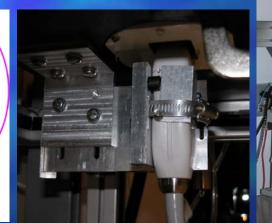
Compliance: indentation

- BioRobotics Lab, Harvard
 - Howe, Kerdok, Jordan
 - ElectroForce TestBench, *in vitro* w/perfusion system; 12mm motion
 - stress relaxation, arbitrary inputs
 - Non-slip suction contact
 - 3-D ultrasound



indenter tip

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ultrasound probe

Scientific Computing Applications in Surgical Simulation of Soft Tissues

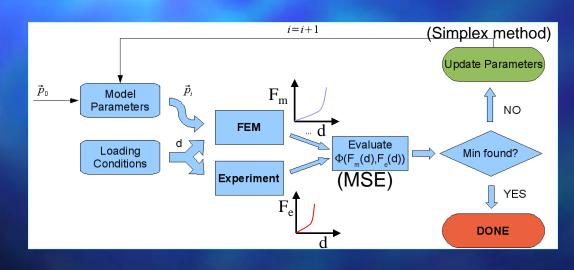
arterial reservoir

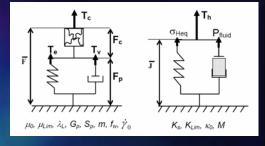


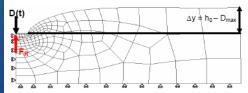
venous reservoir 36

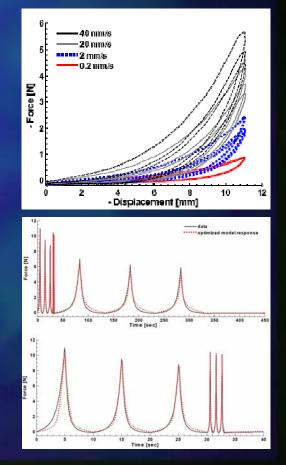
Compliance: parameter extraction

- Parameter identification algorithm
 - iterative FE approach
 - simulate with trial parameters
 - compare with experiment
 - update parameters
 - repeat until convergence









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Compliance: more tissues

- In vitro tests
 - Rodent (rat) liver, kidney
 - NASA Ames/Stanford Virtual Rat Project
 - Bruyns & Ottensmeyer, MICCAI'02)
 - Ovine, bovine, human vocal tissues
 - MGH Ctr. for Laryngeal Surgery & Voice Rehabilitation
 - Testing real tissues to quantify properties to develop compatible biopolymers
 - Porcine brain, muscle/liver
 - In situ cerebral cortex testing
 - Harmonic Motion Imaging (Konofagou et al., Ultrasonics'04)





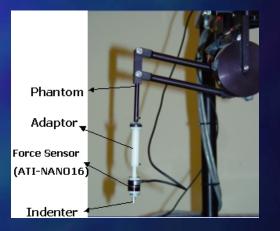




Compliance: indentation tests

- Phantom 1.5 (SensAble) a neat little robot!
 - 125Hz mechanical resonance
 - 190x270x380mm workspace
 - 1.4N continuous force (8.5N max)
- Tendick (UCSF/Berkeley)
 - 20mm hemispherical indenter
 - in vivo porcine stomach/liver/spleen/skin
 - Brower et al., MMVR'01
- Srinivasan (MIT TouchLab)
 - ramp-hold, sinusoidal (0-3Hz) motion
 - 2mm flat cylindrical indenter
 - *in vivo* porcine liver/spleen/kidney/esophagus
 - Kim et al., MICCAI'03, Tay et al., MMVR'02
- De, et al. (RPI)
 - human cadaver measurements, in press

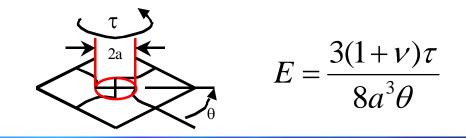




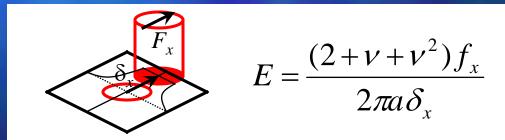
http://touchlab.mit.edu

Compliance: shear tests

- Closed form solutions
 - semi-infinite, non-slip, isotropic, homogeneous, linear
- Torsional shear



Tangential shear



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Compliance: torsional shear

- ROSA2: Kalanovic/Gross (Tuebingen), Ottensmeyer
 - open surgery
 - appl'ns: tissue characterization, surg. sim.
 - 20Hz bandwidth; 30° RoM; 0.45mNm torque
 - 6mm needle/adhesive tip; reference ring 16/20mm ID/OD
 - *in vivo* porcine liver, *in vitro* bovine liver





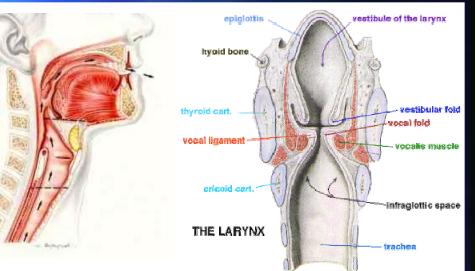


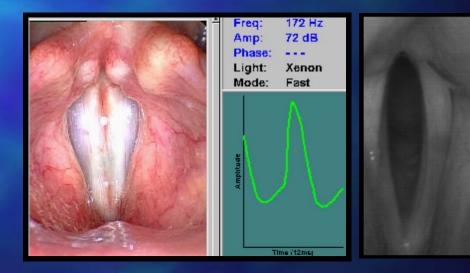


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■ The Larynx

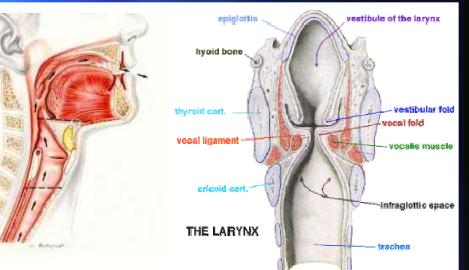
- airflow excites oscillation in vocal folds
- stable, efficient sound production depends on geometry, viscoelasticity





The Larynx

- airflow excites oscillation in vocal folds
- stable, efficient sound production depends on geometry, viscoelasticity



Vocal fold damage

- overuse
- cancer
- Infectious disease



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- Therapeutic concept:
 - Inject/implant biomaterial
 - synthetic gels
 - processed autologous fat
 - Necessary properties
 - long residence time; minimal inflammation, no rejection
 - appropriate mechanical behavior!
 - Two-part challenge
 - measure normal, healthy tissue response
 - measure implant behavior to confirm success

- DeMontfort U., Leicester, UK
 - Goodyer et al. 2006a,b:
 - human in vivo, quasi-static
 - fixed displacement step shear
 - pharmaceutical adhesive bonding
 - G = 0.7-2.2 kPa (possible over-estimate?)

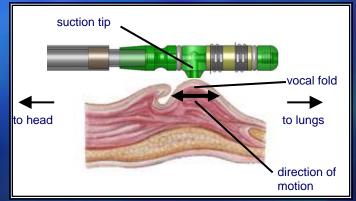


- Early tests with TeMPeST
 - unsuitable for intra-operative use
- Development of VoCCI
 - imposes tangential oscillation, records reaction force.
 - Scotch yoke drive to >250Hz
 - human vocal fundamental from 100-300Hz
 - 50% strain





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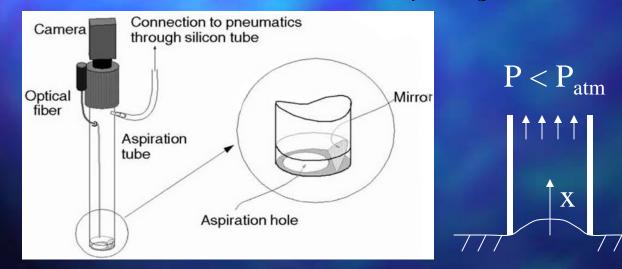
Scientific Computing Applications in Surgical Simulation of Soft Tissues



46

Compliance: *last one!* Aspiration testing

- ETH Zurich, Switzerland
 - Surgical simulation, prediction of cervical incompetance (loss of pregnancy)
 - human cervix in vivo, ex vivo; human liver
 - need for sterility
 - 30Hz frame rate; 3mm displacement observed; 100mbar vacuum; 12mm circular opening

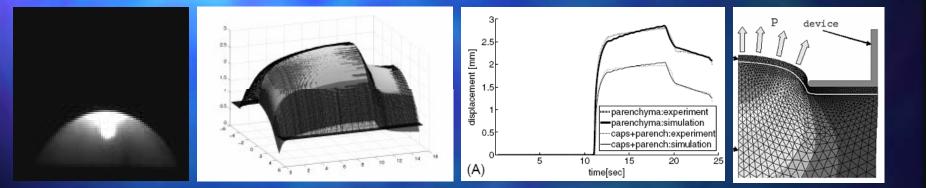




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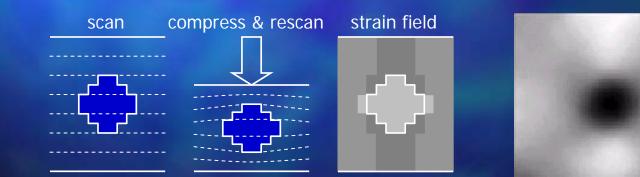
Compliance: aspiration testing

- Hollenstein et al., ISBMS'06
 - stronger pre-conditioning effect ex vivo
 - QLV model with capsule
 - parameter extraction using FEA



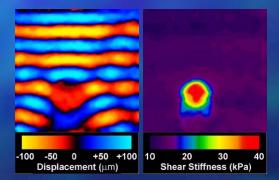
- Imaging techniques
 - Ultrasound
 - Real-time imaging (& inversion)
 - Mechanically deform tissue / focused US shear waves
 - 2-D imaging (with a few exceptions)
 - Estimate 3-D strain tensor
 - Magnetic Resonance Imaging
 - 3-D imaging, arbitrary directions w/equal sensitivity
 - Long scanning/computation times

- Static deformation
 - Ultrasound: Ophir, et al., 1990
 - Magnetic Resonance Imaging: Plewes, et al. 1995
 - US: Scan pre- & post-deformation
 - Normalize, calculate strain & invert
 - Note strain artifacts

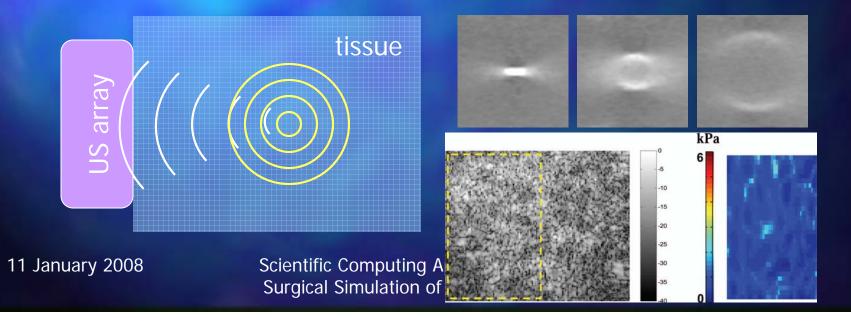


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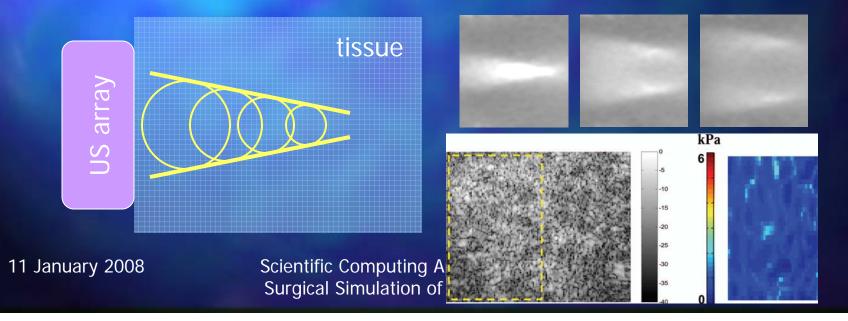
- Dynamic testing: mechanical stimulation
 - Lerner, et al., late '80s: "sonoelasticity imaging"
 - Muthupillai/Manduca/Ehman, ~'95: MRI
 - Mechanical surface vibration (normal or shear)
 - Measure local velocities/amplitude/shear wave velocity
 - Invert amplitude or direct calculation from shear wave velocity
 - $G = v_s^2 \rho$ for Hookean, isotropic medium



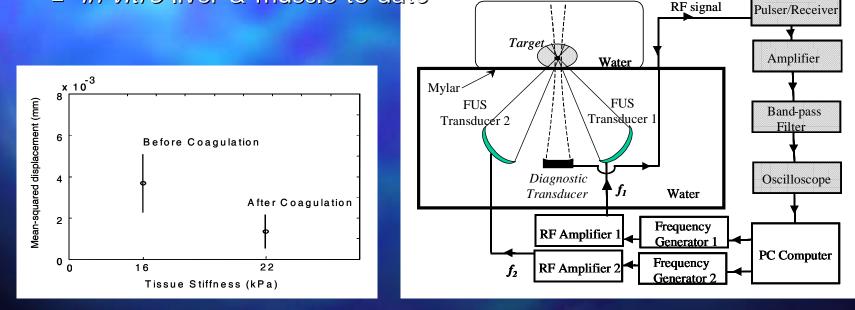
- Dynamic testing
 - Focused ultrasound as stimulus
 - Create local impulse (or train of impulses)
 - Observe traveling shear wave with high frame rate U/S
 - Elasticity related to shear wave velocity
 - Linear viscoelastic model: displacements ~10 μm
 - Fink: Supersonic Shear Imaging: healthy human breast tissue, 1-3kPa Young's mod. (Bercoff et al., IEEE Ultrasonics Symp'03)



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- HMI: Konofagou, et al.; BWH/Columbia
 - *in vitro* so far
 - appl'ns: creating and characterizing lesions in tissue (e.g. tumor ablation)
 - 200 & 800 Hz harmonic force; ~5-10µm amplitude; force not directly measurable
 - in vitro liver & muscle to date



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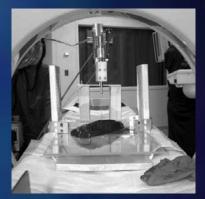
Scientific Computing Applications in Surgical Simulation of Soft Tissues 54

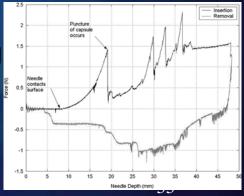
Cutting & Needle Insertion

- More limited data, instruments
- Tendick (Brower et al., MMVR01)
 - measuring tool force on needle driver & scissors
 - 6-dof needle force, 1-dof cutting/spreading
 - 30Hz sampling
 - 3-0 suture through porcine stomach wall,
- Okamura, Haptics Exploration Lab, JHU
 - scissor cutting forces
 - IEEE Trans.Rob.'07, in press
 - percutaneous sim & needle insertion modeling
 - Elastic response, puncture, Karnopp friction
 - Okamura et al., IEEE TBME'04

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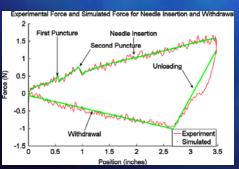


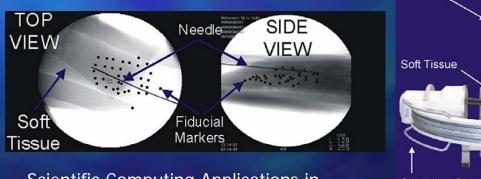


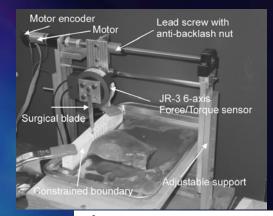
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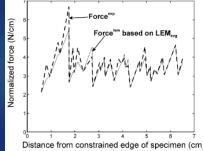
Cutting & Needle Insertion

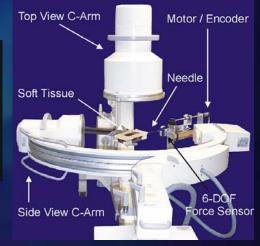
- Desai, RAMS Lab, U.Maryland
 - single blade cutting
 - varying cutting speed, blade angle
 - developed model predicting elastic slope, fracture model
 - Chanthasopeehpan et al., TBME'07a,b
 - needle insertion
 - fluoro imaging of tissue, needle, internal fiducials
 - position/force tracking, porcine tissue in vitro
 - generated simulation w/haptics of needle insertion





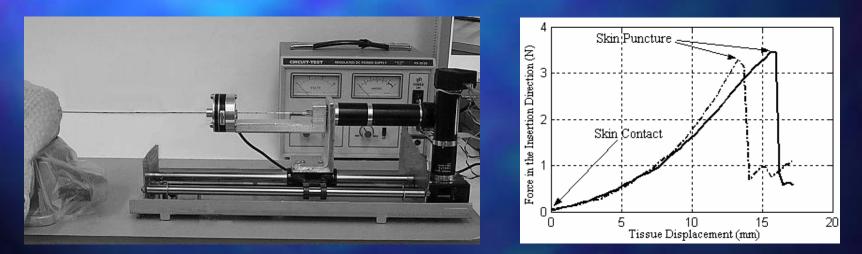






Cutting & Needle Insertion

- U.Western Ontario, Canada
 - Abolhassani, ProcEMBS'04
 - bevelled needle insertion for prostate brachytherapy
 - axial/rotational instrument, 6-DoF force sensing
 - turkey tissue model, insertion rate testing
 - Excellent survey paper: Abolhassani et al., MedEng&Phys'07



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Summary

- Wide range of techniques
 - compliance testing
 - compression, tension, indentation, torsion, aspiration
 - quasi-static to 100Hz—full range of surgical strain rates
 - extremely small to large deformations
 - elastography, coming up, some clinical uses
 - small deformations have questionable application to surg. sim.
 - current applications for diagnostic purposes
 - topology-altering testing
 - needle insertion, scalpel, scissors
 - limited available data
 - growing body of *in vivo* data, including *human*
 - still need more organs, improved constitutive models (& parameters), healthy vs. other conditions...



- AIMS: Advanced Initiatives in Medical Simulation
 - 501(c)(6) non-profit consortium ("lobby group")
 - promotes medical simulation for improving patient safety, reducing errors, ensuring competency, reducing costs...
 - improve awareness, unify the "message", secure resources
 - Enhancing SIMULATION Act, 2007 (H.R.4321)
 - (Safety In Medicine Utilizing Leading Advanced Simulation Technologies to Improve Outcomes Now)
 - reps Forbes (R-VA), Kennedy (D-RI)
- SAVE THE DATE: 5th Annual AIMS Conference & Exhibition
 - May 6-7, 2008, Washington, DC
 - attended by industry, academia, members of congress
- www.medsim.org



- support to develop curricula integrating simulation
- grants to accreditation organizations for standards development
- federal med sim coordinating council
- \$50,000,000 for FY'08, sums as necessary for FY'09-'12
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- ISBMS'08: International Symposium on Computational Models for Biomedical Simulation
 - July 7-8, 2008. London, UK
 - www.imperial.ac.uk/medicine/isbms08
 - Topics of Interest:
 - anatomical modeling; hard & soft biomechanics; physiological models; validation; simulators; haptics; GPU-based sim; etc.
 - 12 March 2008: full papers due (8 page max)
 - successor to IS⁴TM'03 (INRIA), ISMS'04 (CIMIT), ISBMS'06 (ETH)

Scientific Computing Applications in Surgical Simulation of Soft Tissues

ISBMS'08

Society for Simulation in Healthcare



- IMSH'08: International Meeting on Simulation in Healthcare
 - January 13-16, 2008. San Diego, CA
 - www.ssih.org
 - Users, developers, stakeholders in mannequin & computerbased simulators, VR systems, standardized patients, task trainers
 - This year: 1st Technology Track workshop series
 - physical sim development; software-based sim (Harders); cross-platform issues (tissue props, realism, etc.); contact between end users and academic/industrial developers

Questions & further information

www.medicalsim.org www.cimit.org

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Support for some of this work provided by the Department of the Army, grant number DAMD 17-01-1-0667 and by the Institute of Laryngology and Voice Restoration. The ideas and opinions expressed to not necessarily represent those agencies.

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