SLICERMORPH

Introduction to 3D imaging and Morphometrics

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SlicerMorph Core Team:

Co-PI: **Adam Summers** (U. Washington, FHL)
Co-PI: **Doug Boyer** (Duke Evol. Anthropology & Director of MorphoSource.org)
Consultant: **Steve Pieper** (Isomics Co., Chief Software Architect of 3D Slicer)
Lead Developer: **Sara Rolfe** (U. Washington FHL & SCRI)

3DSlicer

A marsupial in Turkey

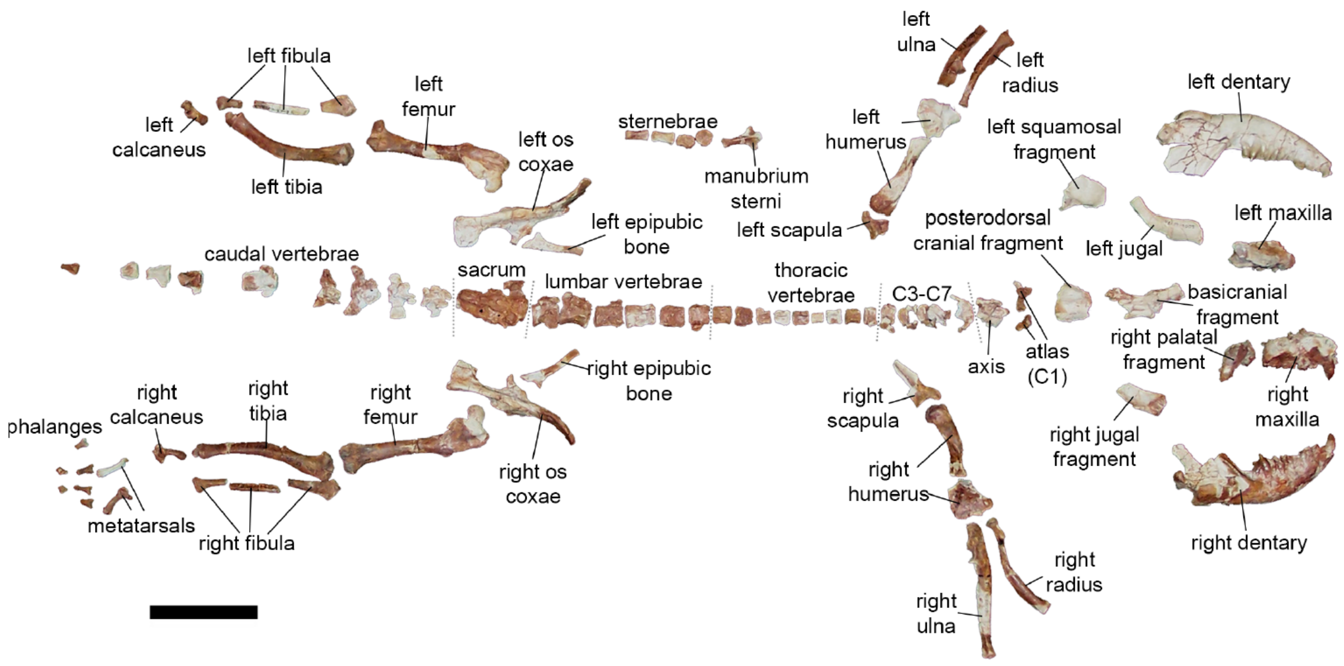

Fig 1. Holotype skeleton of *Anatoliadelphys maasae* (AÜJM 2002–25). Scale bar = 5 cm.

Anatoliadelphys maasae

PLOS | ONE

RESEARCH ARTICLE

Skeleton of an unusual, cat-sized marsupial relative (Metatheria: Marsupialiformes) from the middle Eocene (Lutetian: 44-43 million years ago) of Turkey

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Check for updates

OPEN ACCESS

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Abstract

We describe a near-complete, three-dimensionally preserved skeleton of a metatherian (relative of modern marsupials) from the middle Eocene (Lutetian: 44–43 million years ago) Lülük member of the Uzunçarşıdere Formation, central Turkey. With an estimated body mass of 3–4 kg, about the size of a domestic cat (*Felis catus*) or spotted quoll (*Dasyurus maculatus*), it is an order of magnitude larger than the largest fossil metatherians previously known from the Cenozoic of the northern hemisphere. This new taxon is characterised by large, broad third premolars that probably represent adaptations for hard object feeding (durophagy), and its craniodental morphology suggests the capacity to generate high bite forces. Qualitative and quantitative functional analyses of its postcranial skeleton indicate that it was probably scansorial and relatively agile, perhaps broadly similar in locomotor mode to the spotted quoll, but with a greater capacity for climbing and grasping. Bayesian phylogenetic analysis of a total evidence dataset comprising 259 morphological characters and 9kb of DNA sequence data from five nuclear protein-coding genes, using both undated and "tip-and-node dating" approaches, place the new taxon outside the marsupial crown-clade, but within the clade Marsupialiformes. It demonstrates that at least one metatherian lineage evolved to occupy the small-medium, meso- or hypo-carnivore niche in the northern hemisphere during the early Cenozoic, at a time when there were numerous eutherians (placentals and their fossil relatives) filling similar niches. However, the known mammal fauna from Uzunçarşıdere Formation appears highly endemic, and geological evidence suggests that this region of Turkey was an island for at least part of the early Cenozoic, and so the new taxon may have evolved in isolation from potential eutherian competitors. Nevertheless, the new taxon reveals previously unsuspected ecomorphological disparity among northern hemisphere metatherians during the first half of the Cenozoic.

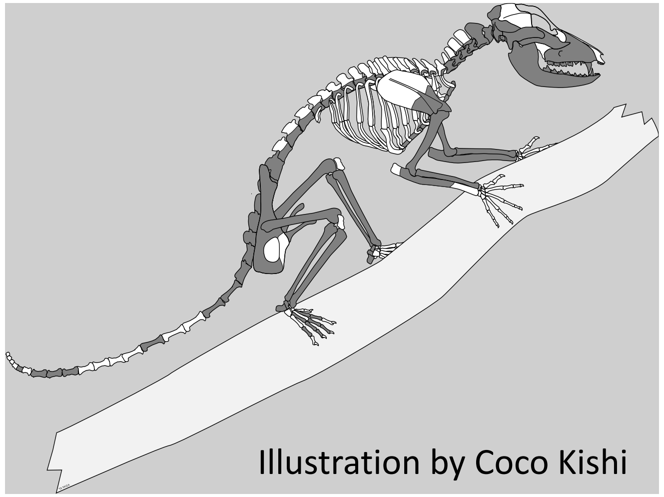
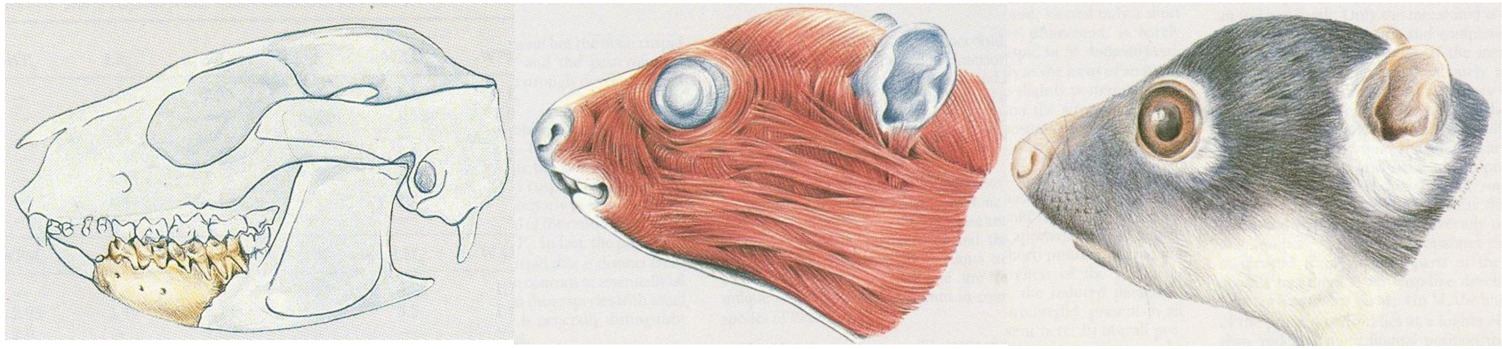


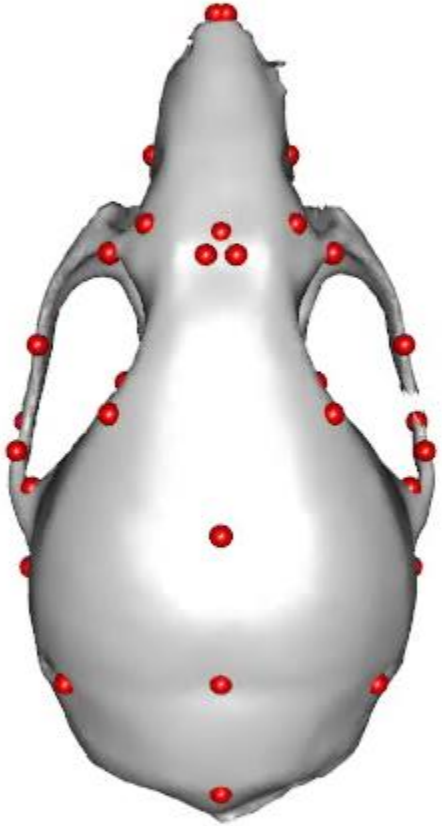
Illustration by Coco Kishi

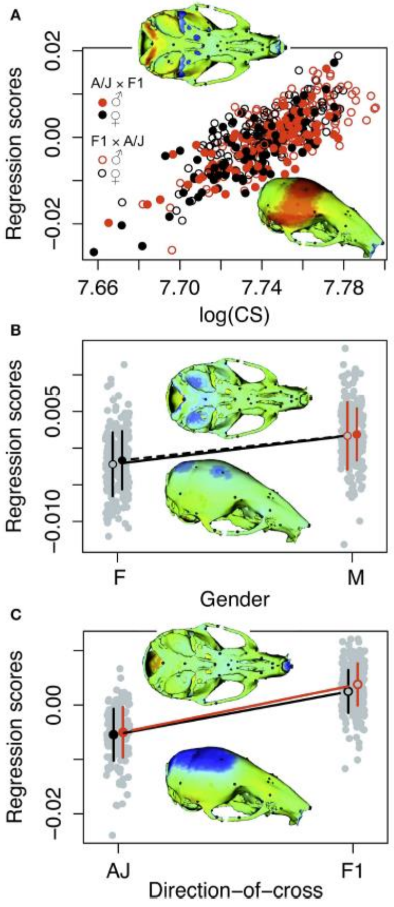
Illustration by Peter Schouten

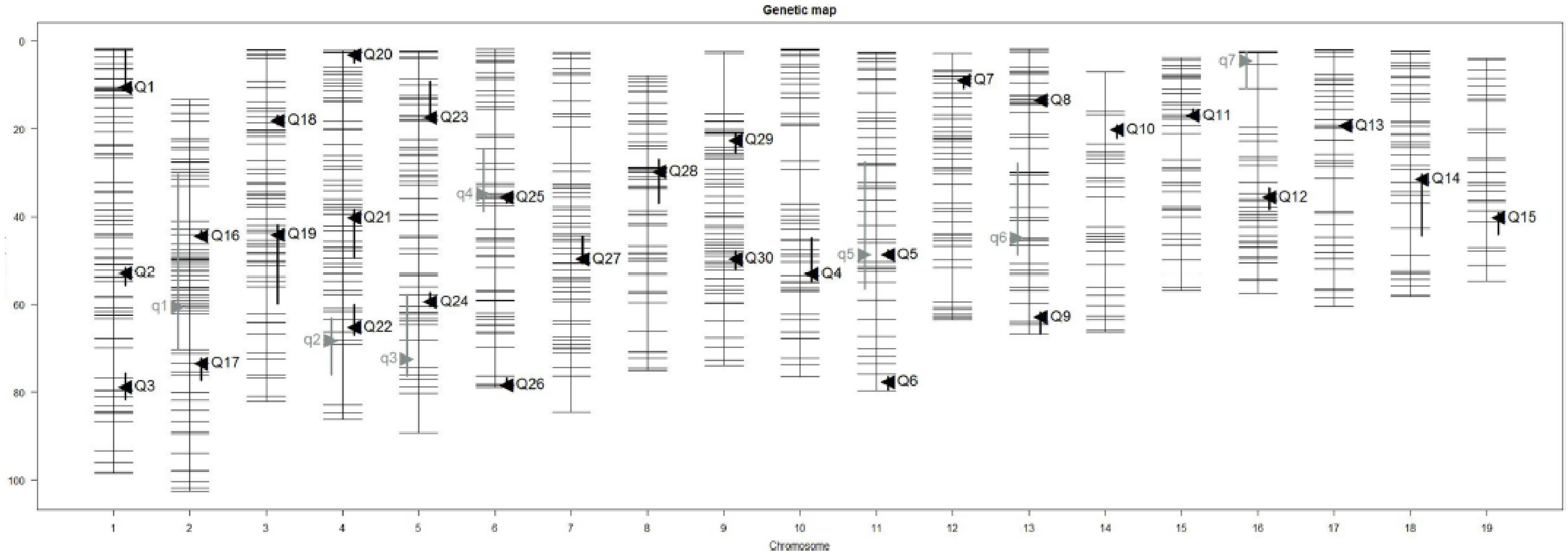


Woodburne et al. 1987. New Miocene ringtail possums from South Australia

Unfolding the genotype/phenotype map in craniofacial system

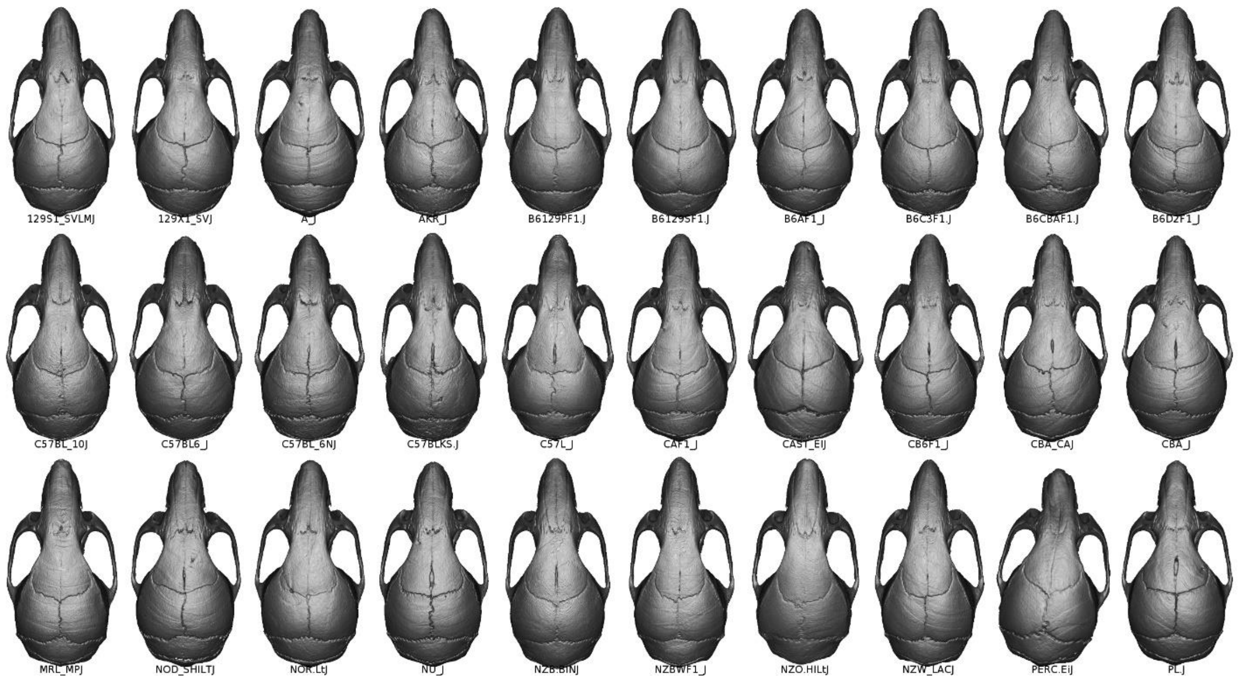


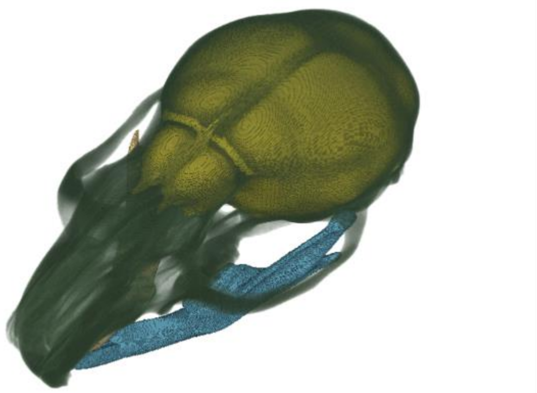


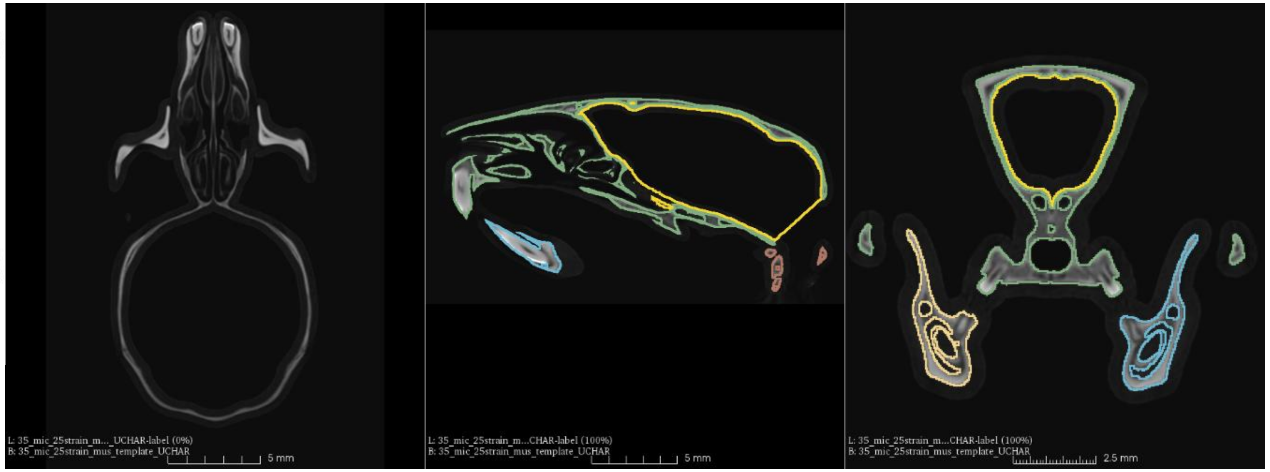


- Maga AM, et al. 2015. Quantitative trait loci affecting the 3D skull shape and size in mouse and prioritization of candidate genes in-silico. *Frontiers in Physiology | Craniofacial Biology* 6:92.
- Navarro N, Maga AM. 2016. Does 3D Phenotyping Yield Substantial Insights in the Genetics of the Mouse Mandible Shape? *G3: Genes, Genomes, Genetics* 6:1153–1163.
- Navarro N, Maga AM. 2018. Genetic mapping of molar size relations identifies inhibitory locus for third molars in mice. *Heredity* 121:1–11.

Image-based analysis (registration & segmentation)

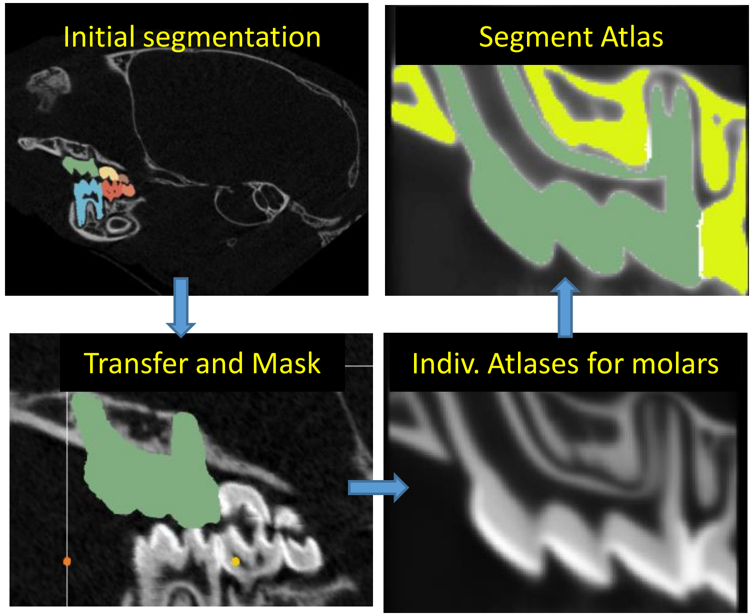


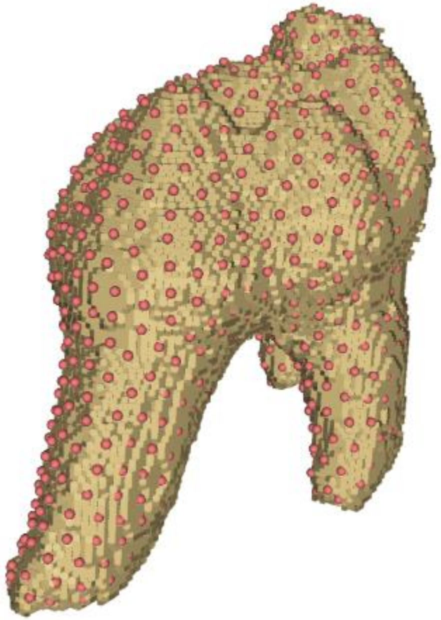


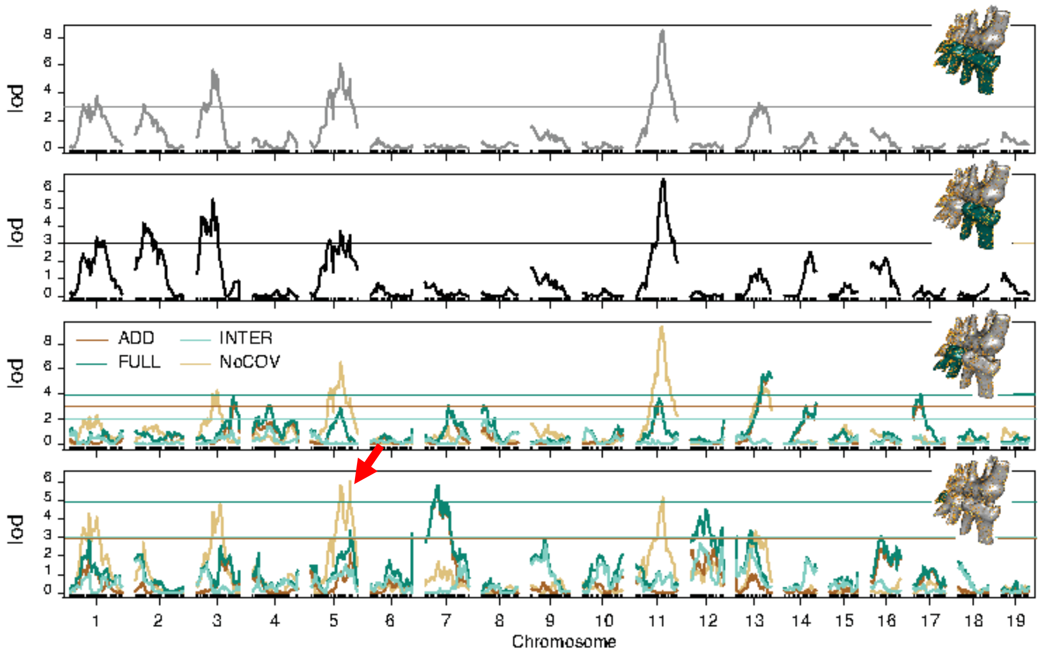


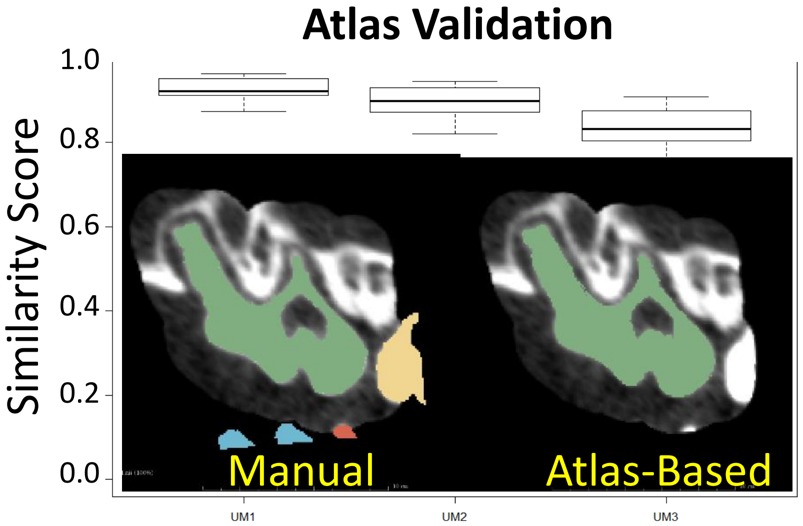
- Young R, Maga AM. 2015. Performance of single and multi-atlas based automated landmarking methods compared to expert annotations in volumetric microCT datasets of mouse mandibles. Frontiers in Zoology 12:33.
- Maga AM, Tustison NJ, Avants BB. 2017. A population level atlas of *Mus musculus* craniofacial skeleton and automated image-based shape analysis. *Journal of Anatomy* 231:433–443.

Genetic control of 3D molar size





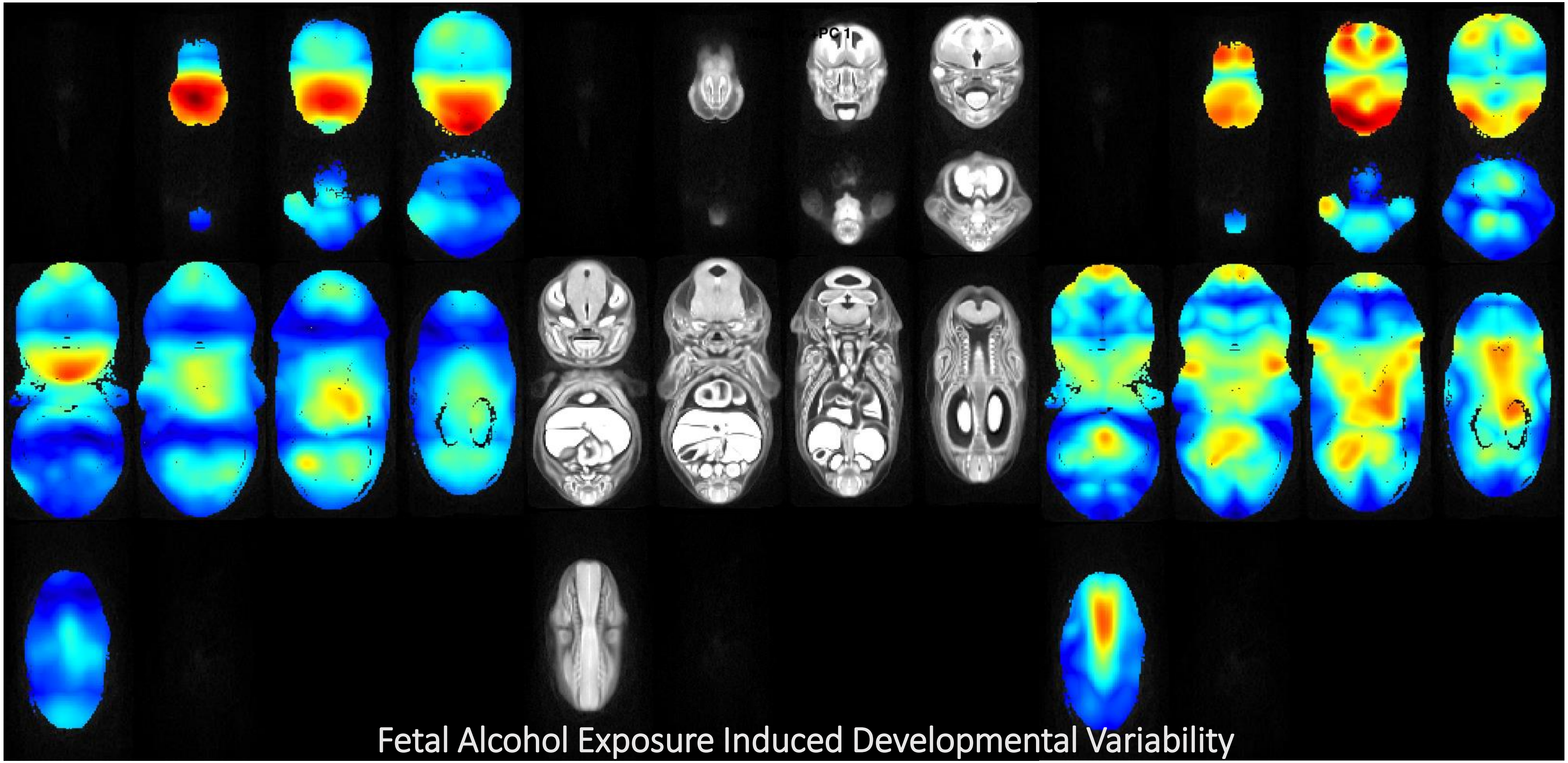




Pipeline for automated segmentation of 2,500 molars from more than 400 mouse scans

- Navarro N, Maga AM. 2018. Genetic mapping of molar size relations identifies inhibitory locus for third molars in mice. *Heredity* 121:1–11.

PCA as a tool for exploratory analysis in mouse screens



Control mice fetuses at E15

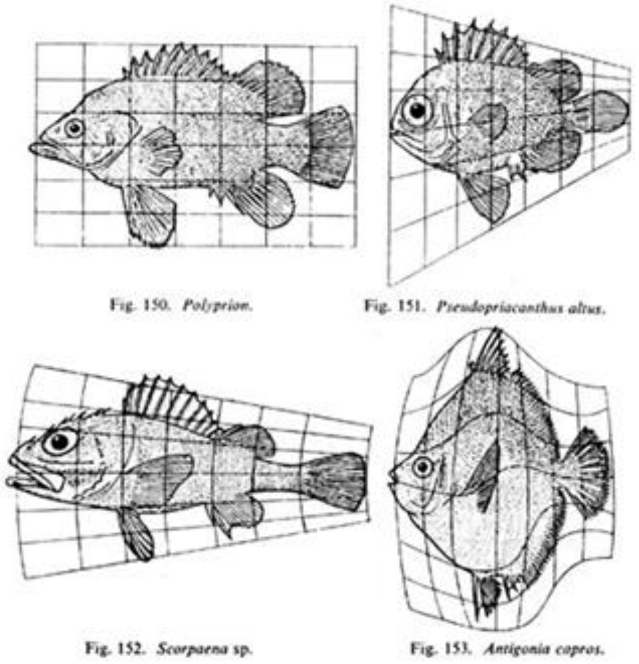
Maga lab unpublished data (undergrad project)

Study template

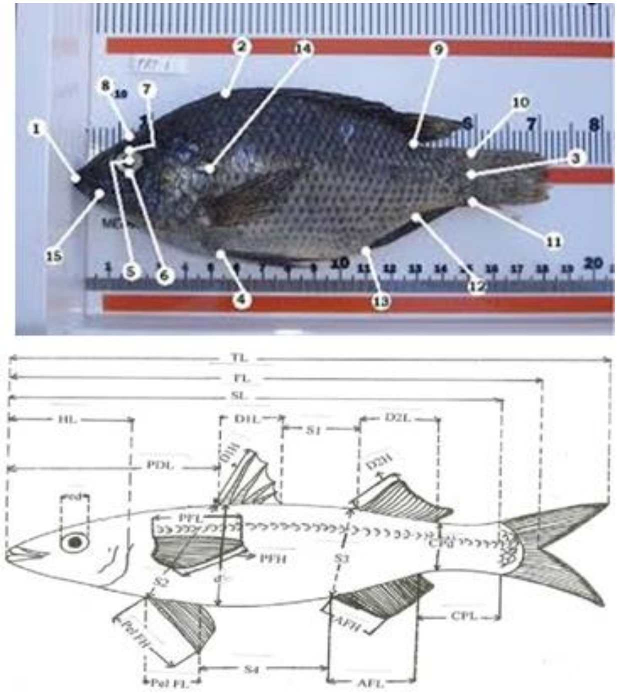
(Population average)

E15 fetuses from dams consumed 10% v/v EtOH *ad-libidum* during the first 8 days of pregnancy (E0-E8)

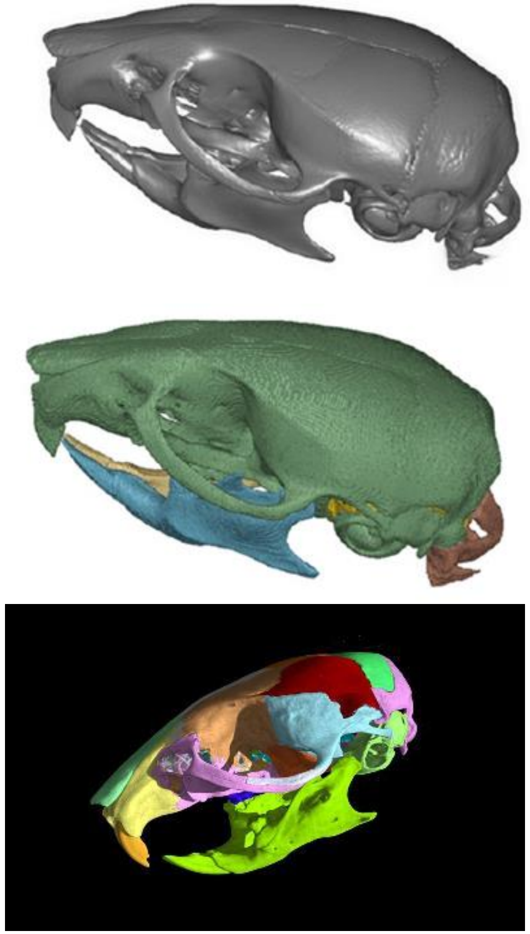
Moving beyond state-of-art and why now?



1900s

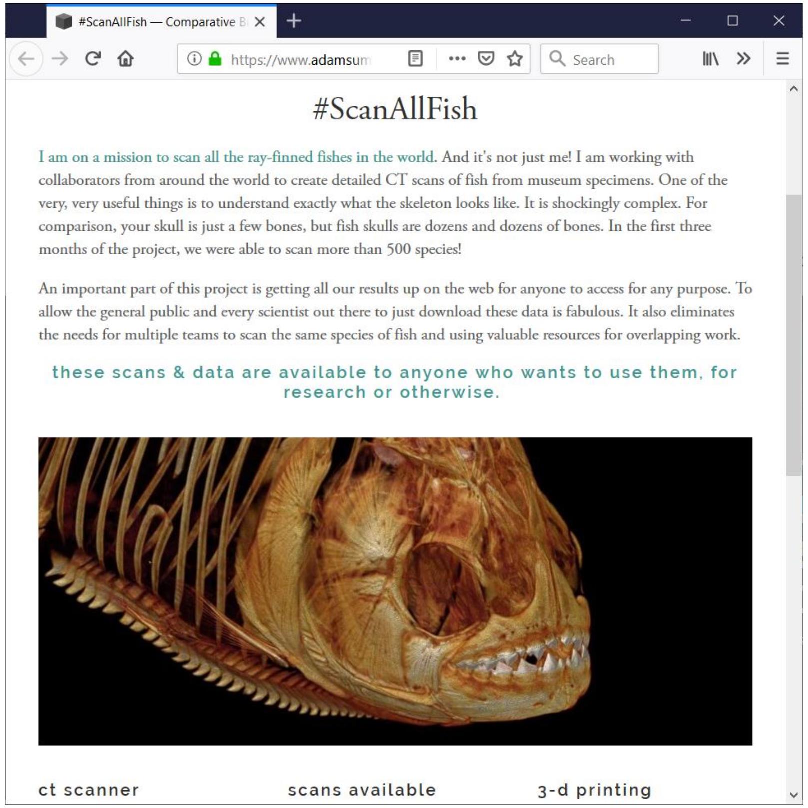


1990s-2010s

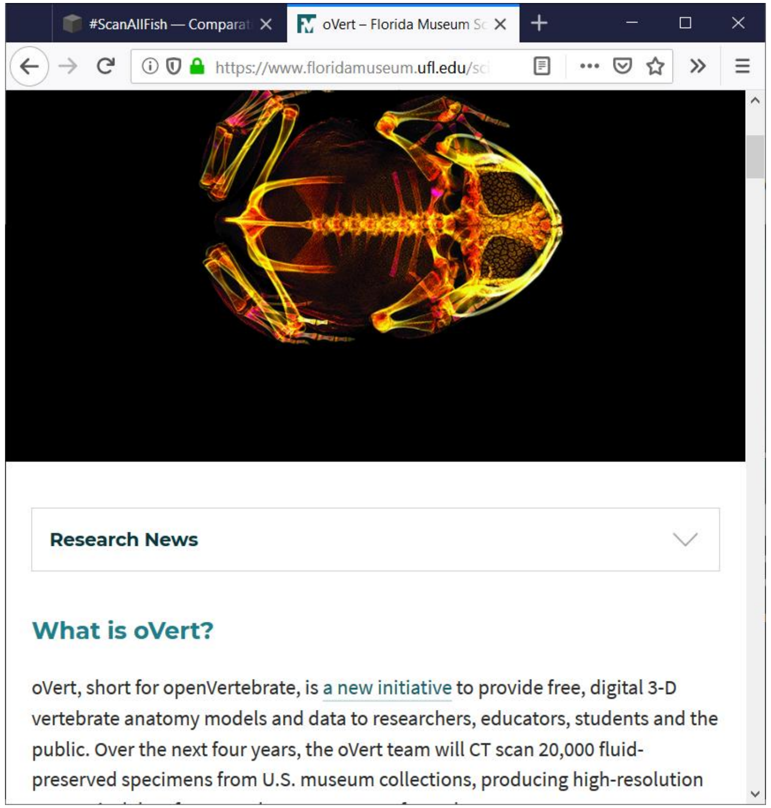


2010s-

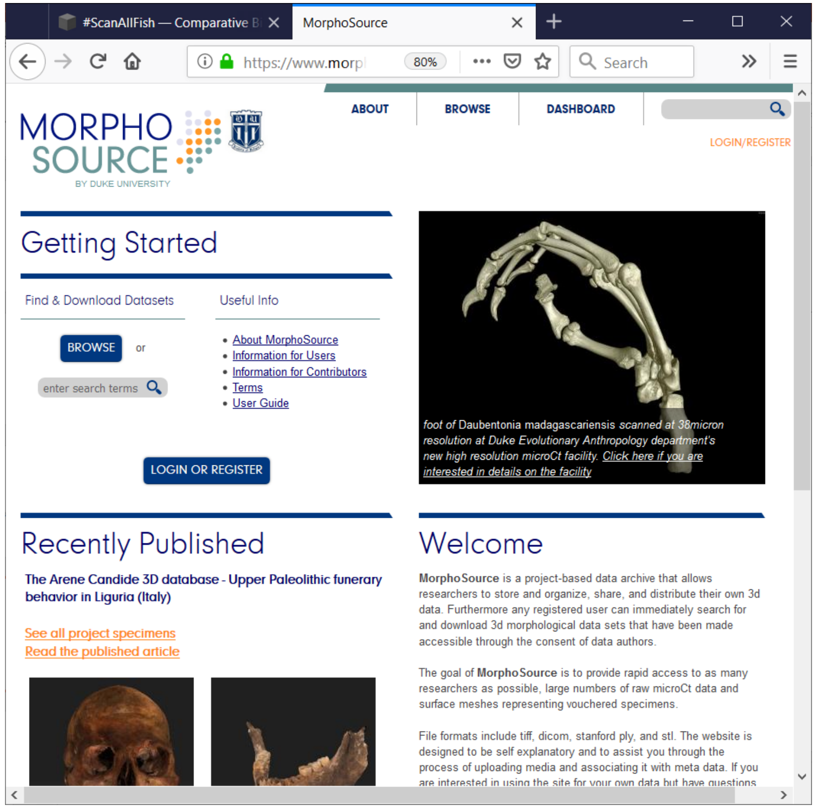
The final frontier



#ScanAllFishes



Open Vertebrate



MorphoSource.org

Morphometrics discussion list

https://groups.google.com/forum/#!forum/morphmet2

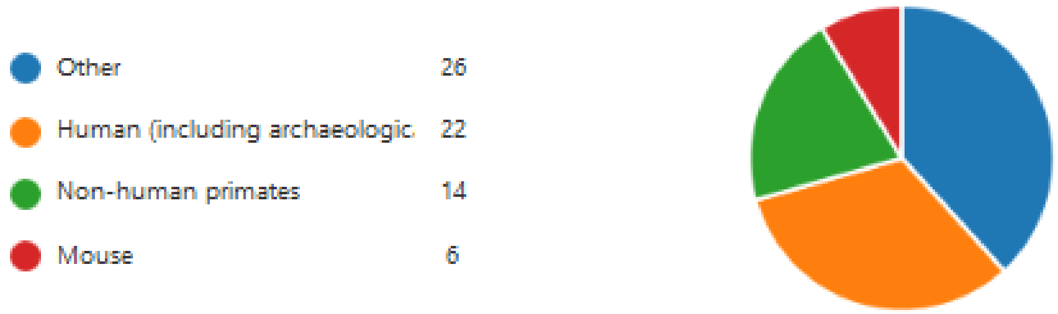
- ~1000 members from a global pool of scientists interested in using quantitative methods to analyze organismal shape and form.
- Diverse body of interests: Ecologists, evo/devo biologists, systematists, paleontologists, anthropologists and biomedical researchers.
- Motivating question: "**I want to analyze shape variation patterns in XYZ species... I found datasets in MorphoSource / DigiMorph etc….., but don't know what to do**".

Survey of 3D morphometrics

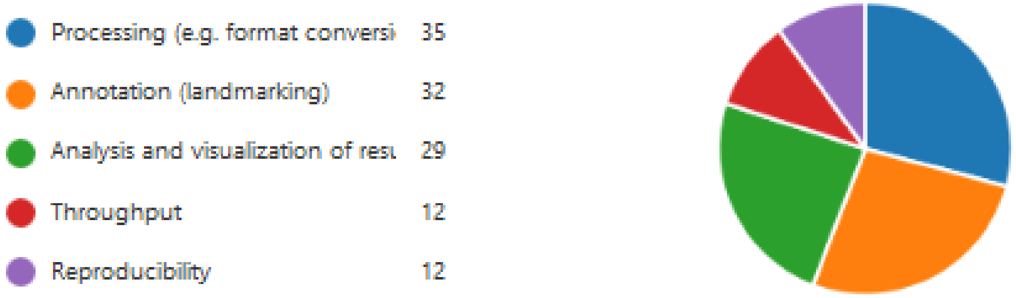
- A survey for people who are working (or planning to work) with volumetric datasets (CT, MR, and likes).
- Challenges identified were:

1. Data wrangling (converting formats)
2. Annotation (measurements)
3. Analysis and visualization

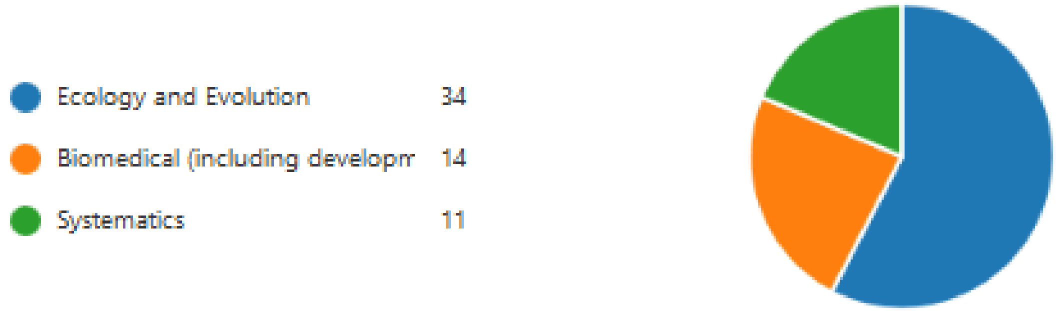
2. What organism are you working on? (choose multiple if need)



5. What are your challenges working with these data? (choose multiple if need



3. What is your main research focus ? (choose multiple if need)



A typical workflow:

1. Download data from one or more of the repositories in different formats and/or modalities.
2. Find a software that will enable 3D visualization/segmentation and conversion to mesh, then landmark digitization (commercial software like Aviso, Mimics, Geomagics, Analyze, or free ImageJ, 3D Slicer, ITK-Snap)
3. Export landmark data into a format that can be understood by the analysis software.
4. Analyze using R (or MorphoJ)
5. Export results back to the digitization software to visualize

Let’s fix that! (Thank you NSF!)

1. Find your data, download, visualize, segment, animate, measure, annotate, vet your landmarks, and construct your basic morphospace in **SlicerMorph**. Then, export result for:
2. Domain-specific analysis (symmetry decomposition, phylogenetic PCA, linear models, covariation) in R (geomorph, Morpho, etc).

SlicerMorph Project Organization

- **SlicerMorph Core Team:**
  - Lead-PI: **Murat Maga** (UW / Seattle Children's)
  - Co-PI: **Adam Summers** (UW FHL)
  - Co-PI: **Doug Boyer** (Duke Evol. Anthropology & Director of MorphoSource.org)
  - Consultant: **Steve Pieper** (Isomics Co., Chief Software Architect of 3D Slicer)
  - Lead Developer: **Sara Rolfe** (UW FHL & SCRI)

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- **SlicerMorph Advisory Committee:**
  - James Rohlf (Stony Brook U)
  - Dean Adams (Iowa State U)
  - David Polly (Indiana U)
  - Anjali Goswami (Natural History Museum, London)

Collaborative Proposal: ABI Development: An Integrated Platform for Retrieval, Visualization and Analysis of 3D Morphology From Digital Biological Collections (ABI 1759883, 1759637, 1759839) 08/01/2018-07/31/2021
https://nsf.gov/awardsearch/showAward?AWD_ID=1759883&HistoricalAwards=false

SlicerMorph Road Map

- **Already in the extension**
  - Generalized Procrustes Analysis (GPA) and PCA visualization of shapes, plotting
  - Data import tools (IDAV Landmark, morphologika, Bruker/Skyscan)
  - Browse MorphoSource within SlicerMorph.
- **Work-in-progress, or SlicerMorph Labs: (Now – 2021)**
  - Semi-landmarking tools (patch-based, curve-based, soon spherical template)
  - Transfer landmarks from a template or connectivity grid.
  - General-purpose image stack import (ImageStacks)
  - Basic keyframe based animations (SlicerAnimator)
  - Implement landmark-free correspondence (auto3Dgm) between shapes (Duke)
  - Optimize the GPA UI and performance.
- **SlicerMorph v2 (if funded, 2021 –)**
  - Cloud-based computational resources
  - Community hub for data and idea exchange
  - Tighter integration with R (e.g., Morpho, GeoMorph)

We are essentially a bridge between the core Slicer Developers and biosciences community.

SlicerMorph User Training and Support

- **Three more SlicerMorph 3D Morphometrics short-courses:**
  - August 22-29, 2020 Summer short-course (announcement in April)
  - Two dates in 2021 (TBD)
- **Day workshop/tutorials at professional meetings:**
  - SICB 2021 (DC)
  - AAPA 2021 (Philadelphia)
- **Onsite (invited) workshops**
- **Starting March, online, interactive office hours:**
  - 4th Wednesday of each month 11-12p (PDT)
  - First meeting March 24th, 2020
  - http://bit.ly/maga_webex
- **Community support at https://discourse.slicer.org (use SlicerMorph tag)**

SlicerMorph vs 3D Slicer

SlicerMorph is 3D Slicer customized. Its bundled with morphometrics extensions and additional modules we find that are useful for workflows around organismal biology. It contains:

1. Our SlicerMorph project specific modules (these are also in official extension):
   - Generalized Procrustes Analysis
   - Bruker/Skyscan dataset import
2. WIP modules from the 'SlicerMorph Labs'
   - Semi-Landmarks (template creation and transfer)
   - SlicerAnimator
   - ImageStack import
   - Auto3Dgm
3. Other extensions and modules that are not part of core 3D Slicer functions
   - Image Guided Therapy Extension offers Fiducial (Landmark Registration)
   - Sandbox offers Curved Planar Reformat (aka unbending) and RawImageGuess (to import undocumented data formats, e.g., from VGStudio Max)

Workshop Resources

- **SlicerMorph website**: http://SlicerMorph.org
- **Sign up for announcements' and updates**: http://bit.ly/SM-listserv
- **Follow us on Twitter:** @SlicerMorph
- **Course lectures and labs**: https://github.com/SlicerMorph/W_2020
- **Youtube channel for video tutorials**: http://bit.ly/SM_youtube
- **SlicerMorph download link:** http://download.slicermorph.org
- **Download sample data:**
  - https://app.box.com/s/b67kkwc8od43u8lmiuzw01ns5gwc5fcq

Overview of the week

	2/16	2/17	2/18	2/19	2/20	2/21	2/22	2/23
7:45-8:15		Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	Brunch / Checkout
8:30-10:15		**Introduction** Maga **3D imaging** Summers	**Applied Imaging Concepts** Rolfe	**Introduction to Statistical Shape Analysis II: Semi-Landmarks and beyond** Rolfe	**Auto3Dgm and landmark-free correspondence of biological form** Shan	**TBD**	**Work on your on data / TBD**	
10:15-10:30		Coffee Break	Coffee Break	Coffee Break	Coffee Break	Coffee Break	Coffee Break	
10:30-12:15		Attendee project Presentations - Initial	**Slicer #3: Segmentation, mesh conversion** Maga	**SlicerMorph # 1: Statistical Shape Analysis: Work with sample data** Maga	**Auto3Dgm: Establishing Landmark-free correspondence** Shan	**Repetitive tasks, Scripting in Slicer** Rolfe	**Work on your on data / TBD**	
12:15-12:45		Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	
1:00-3:00	Course check-in & Self-Paced Pre Course Lab (Dining Hall)	**Slicer #1: UI, overview of functionality, extensions, finding help** Mercan	**Introduction to Statistical Shape Analysis I: Landmark-based methods** Maga	**Template-based analysis and computational anatomy** Maga	**Application of SSA: Modeling growth** Mercan	**Building Statistical Shape Models in R** Schlager	**Setting your own lab / Concluding remarks** SlicerMorph team	
3:00-3:15		Coffee Break	Coffee Break	Coffee Break	Coffee Break	Coffee Break	Coffee Break	
3:15-5.15		**Slicer #2: Data formats, getting data from M/S, saving** Maga	**Slicer #4: Measurements and Visualization** Rolfe	**SlicerMorph # 2: Statistical Shape Analysis: Work on your data**	**Integrating SlicerMorph with R** Mercan	**Data processing in R: Plotting, modeling** Schlager	Visualization Competition and Social	
6:00-6:30	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	
7:00-8:00		Smores on beach	Study Hall @Dining Hall -	Study Hall @Dining Hall -	Study Hall @Dining Hall -	Study Hall @Dining Hall -		

EVALUTIONS

- **Evaluation forms:** We need your feedback both right at the end of each lecture and lab. Please find the online surveys for each lab and lecture at: **https://github.com/SlicerMorph/W_2020/blob/master/Evaluations.md**
- A final survey for overall course feedback at the end (Saturday PM). Same link as above.
- Critical for our renewal and continuation efforts.

Today: Lightning Talks (5 minutes max, 3-4 slides)

PLEASE REMEMBER to UPLOAD them https://faculty.washington.edu/maga/data_dropbox/

*** S’mores on the beach tonight after dinner.**
(wait for updates on transportation)

*** Rowboat orientations on Tuesday @10**
Two sessions: 10-10.15, or 10.15-10.30

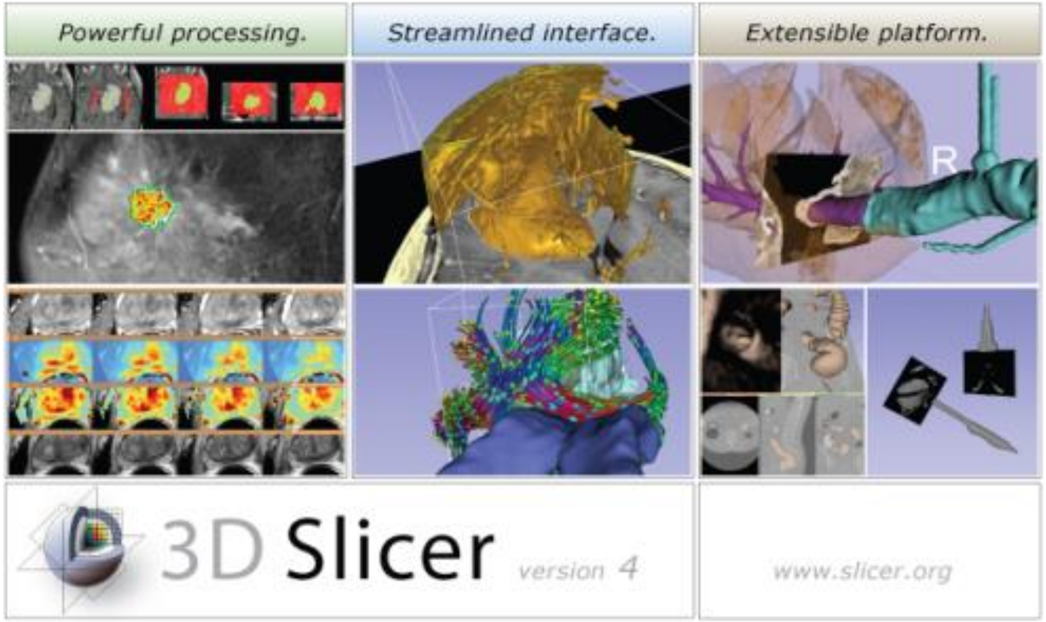
*** Social and visualization showdown**
Saturday PM

Slicer/SlicerMorph Champions

- Be the resident-expert. Share what you learn with your lab mates.
- Write and share SOPs on the SlicerMorph website (it is a git repository after all!)
- Develop tutorials/use cases.

Background for 3D Slicer

- Software application for medical image computing: data import/export, visualization, segmentation, registration, quantification, real-time guidance
- Application framework: customizable, extensible custom modules
- Completely free (BSD)
- Multi-platform



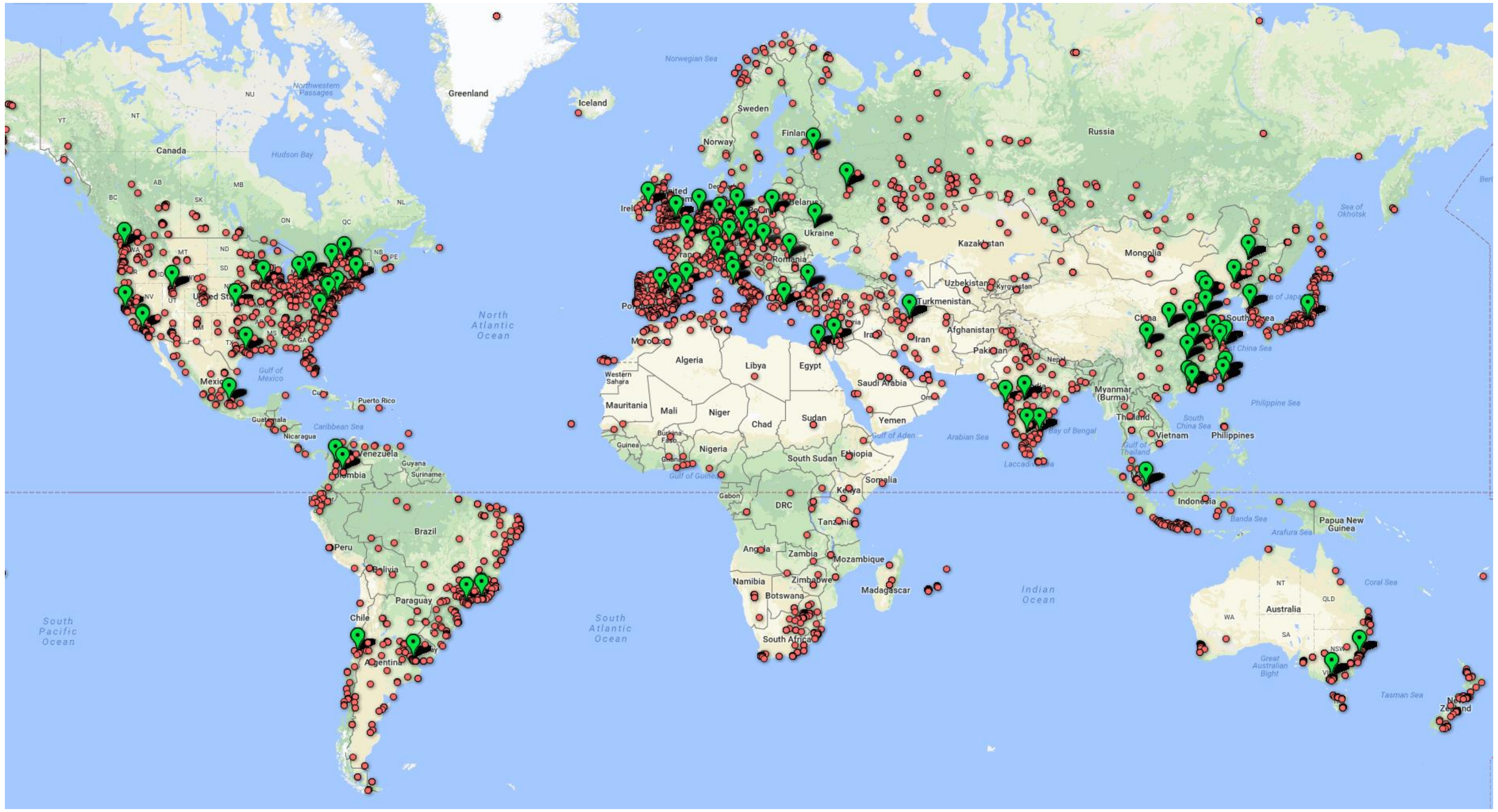
- User and developer support
- Training courses, documentation, tutorials

Fedorov, *et al.* "3D Slicer as an image computing platform for the Quantitative Imaging Network." Magnetic resonance imaging 30.9 (2012): 1323-1341.

Large user community

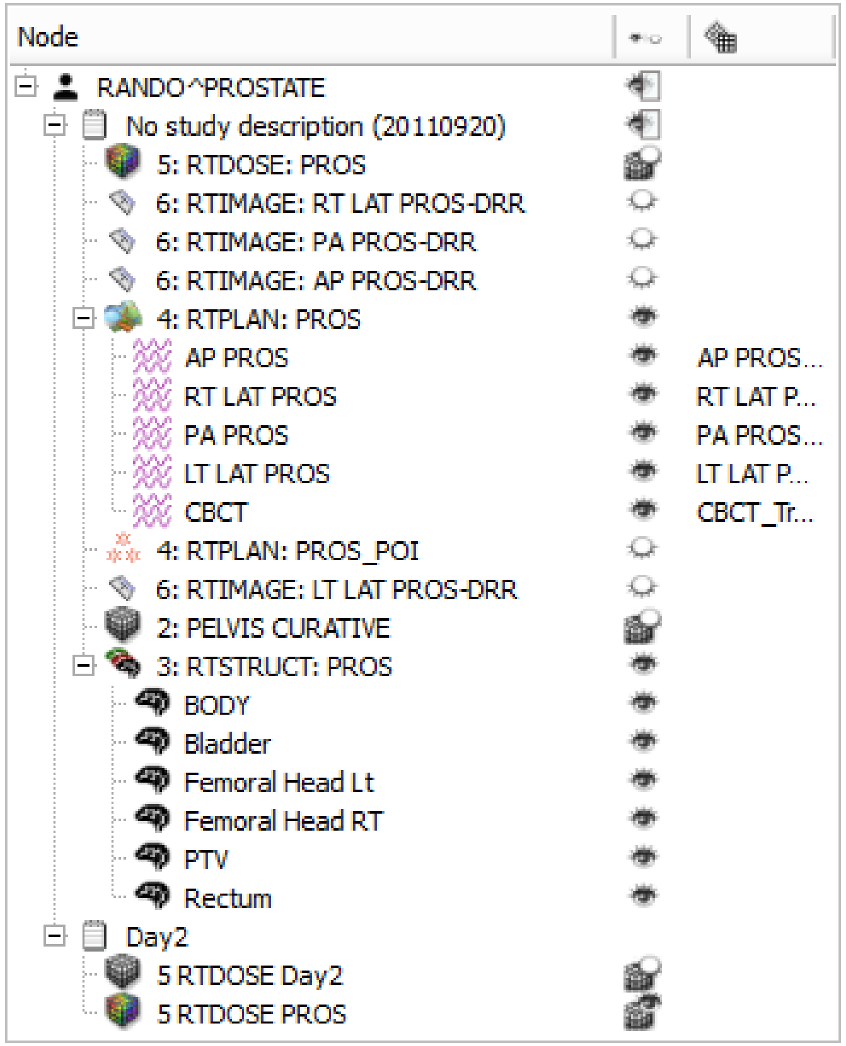
500 downloads per week in 2012
2800 downloads per week in 2018

330 000+ downloads over the past 5 years:



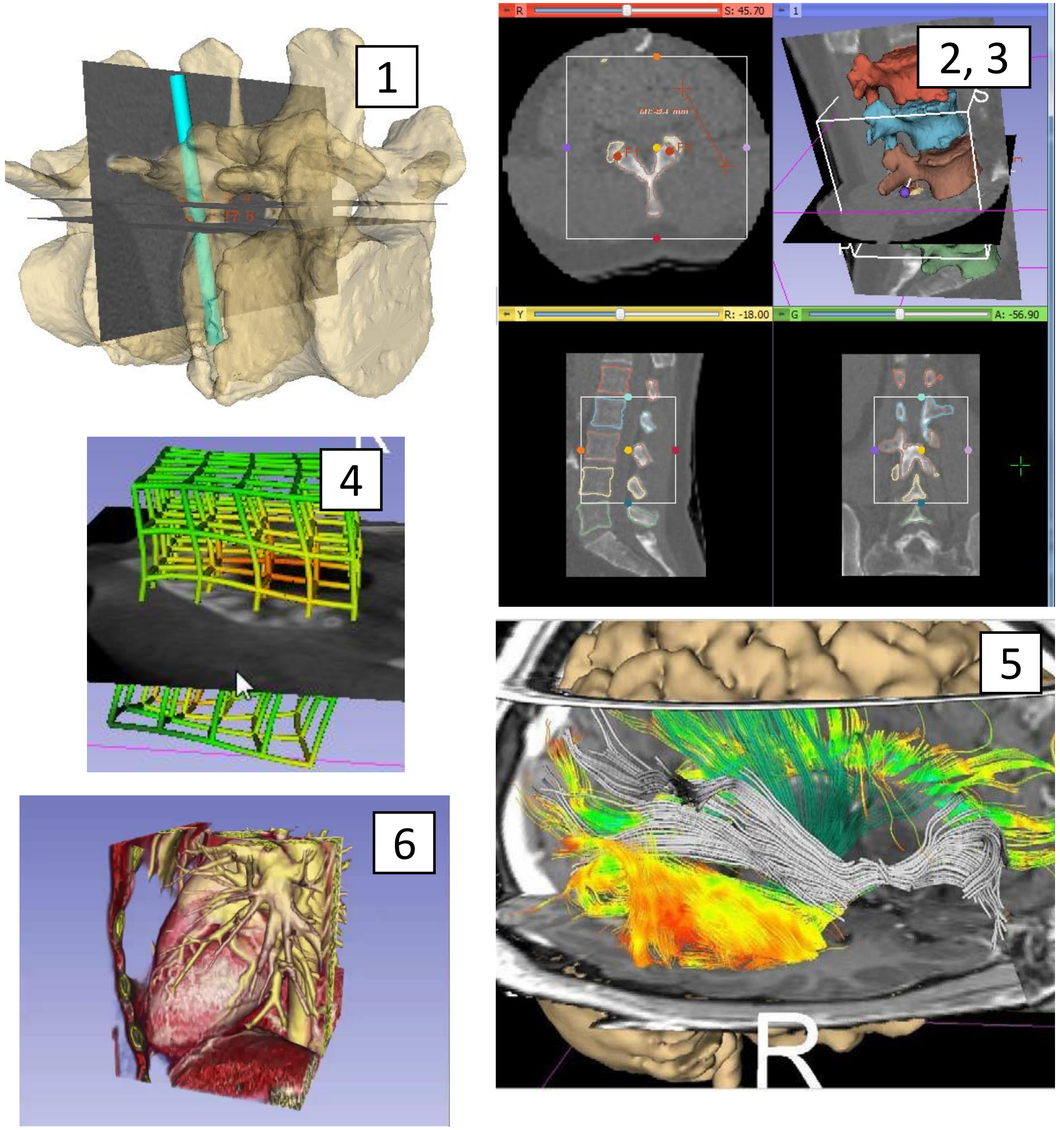
Data import/export

- DICOM: 2D/3D/4D volumes, structure sets, dose volumes, etc. (extensible without Slicer core changes)
- Research data formats for volumes, meshes, transforms (NRRD, MetaIO, VTK, HDF, etc.)
- Common non-medical data formats (JPEG, TIFF, etc.)
- Save and complete restore of application state



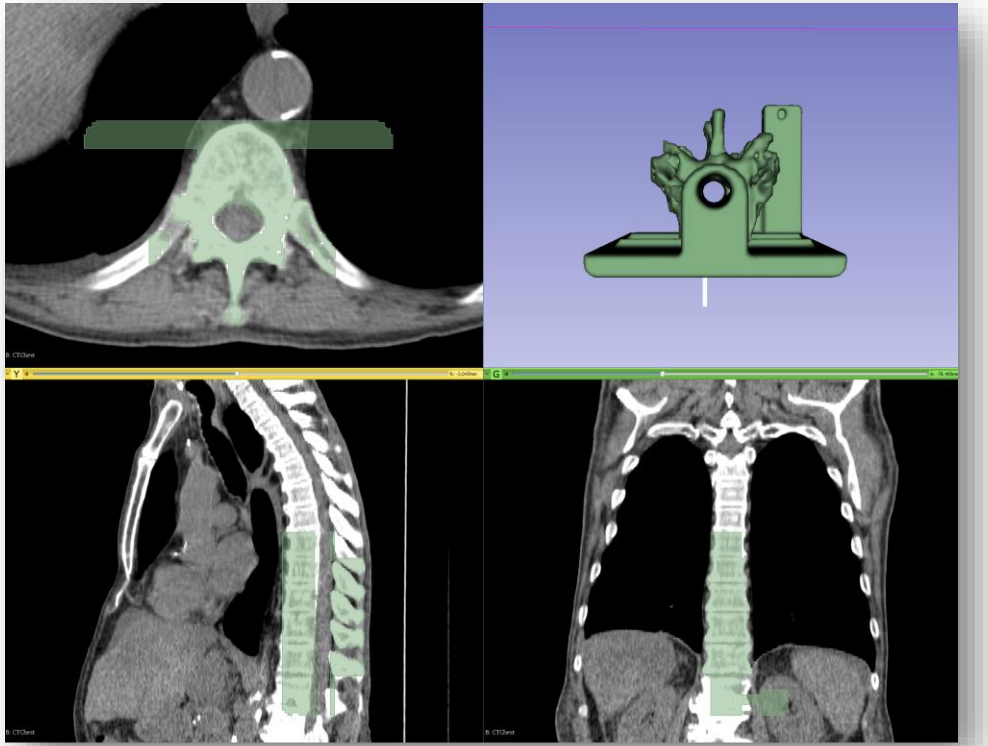
Extensive Visualization Capabilities

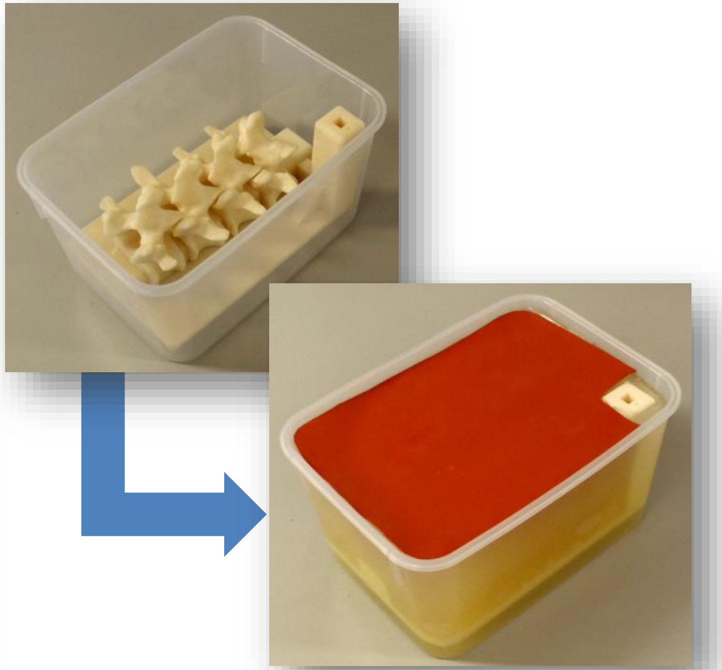
1. 2D (slice) and 3D views, chart views
2. Configurable layout
3. Multi-modality image fusion (foreground, background, label map)
4. Transforms, vector and tensor field visualization
5. Surface and volume rendering
6. Time sequence data



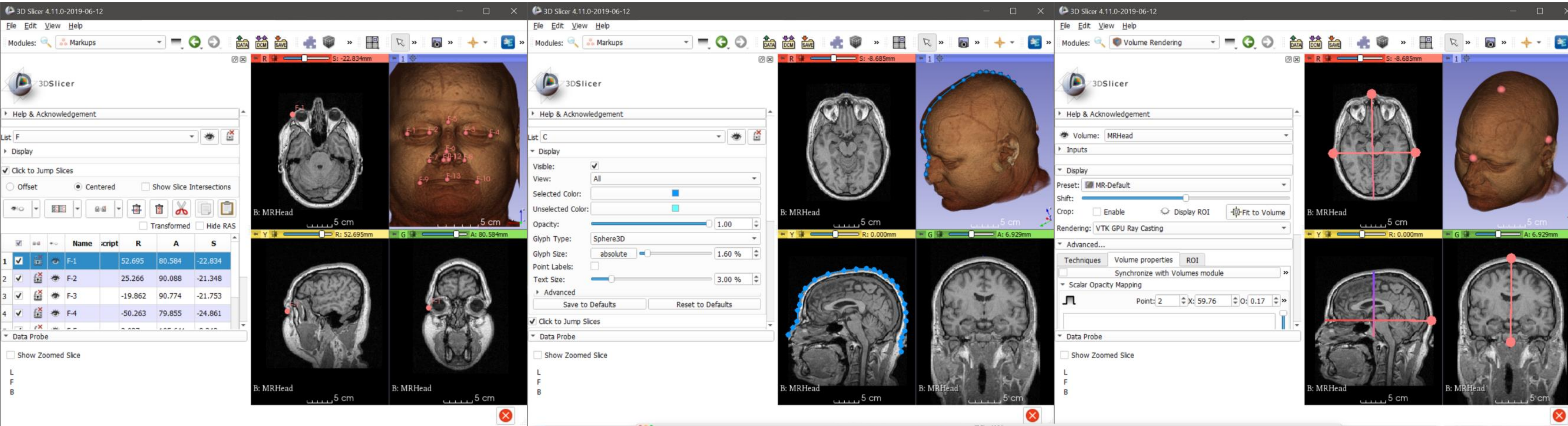
Segmentation

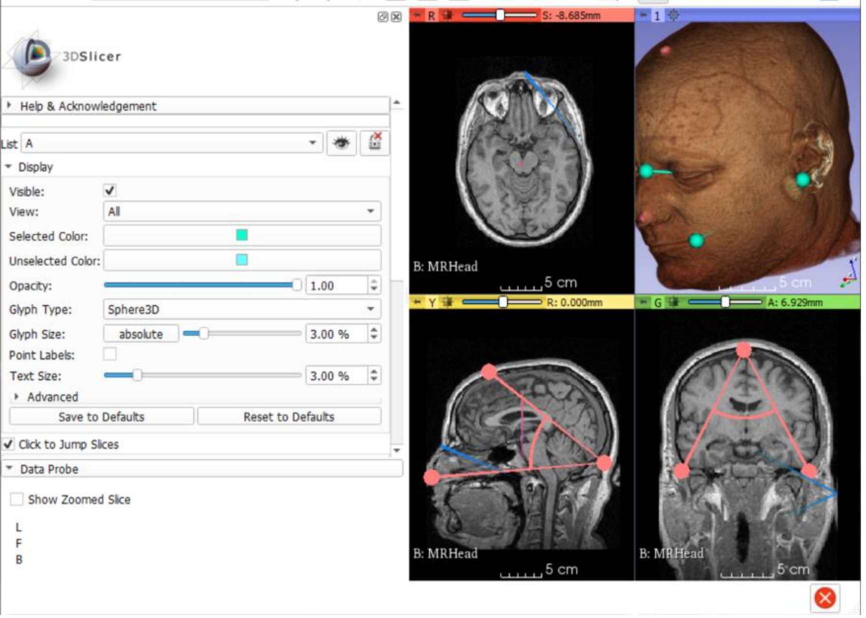
- Manual (paint, draw, scissor, threshold, etc.)
- Semi-automatic (region-growing, fill between slices, etc.)
- Automatic (atlas-based, robust statistics, etc.)

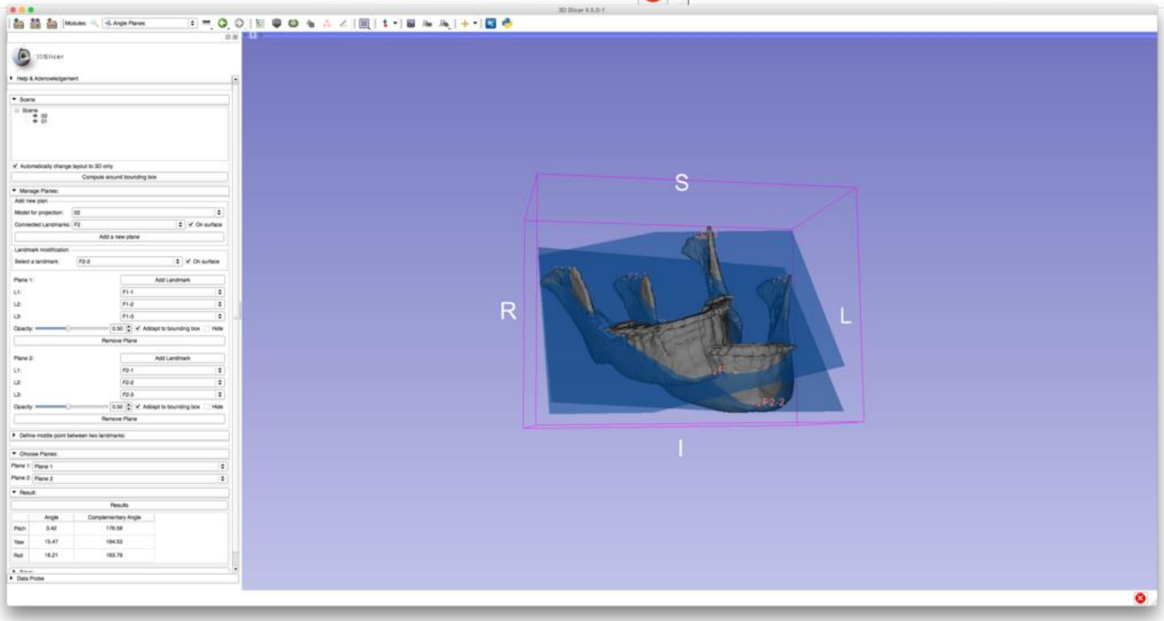




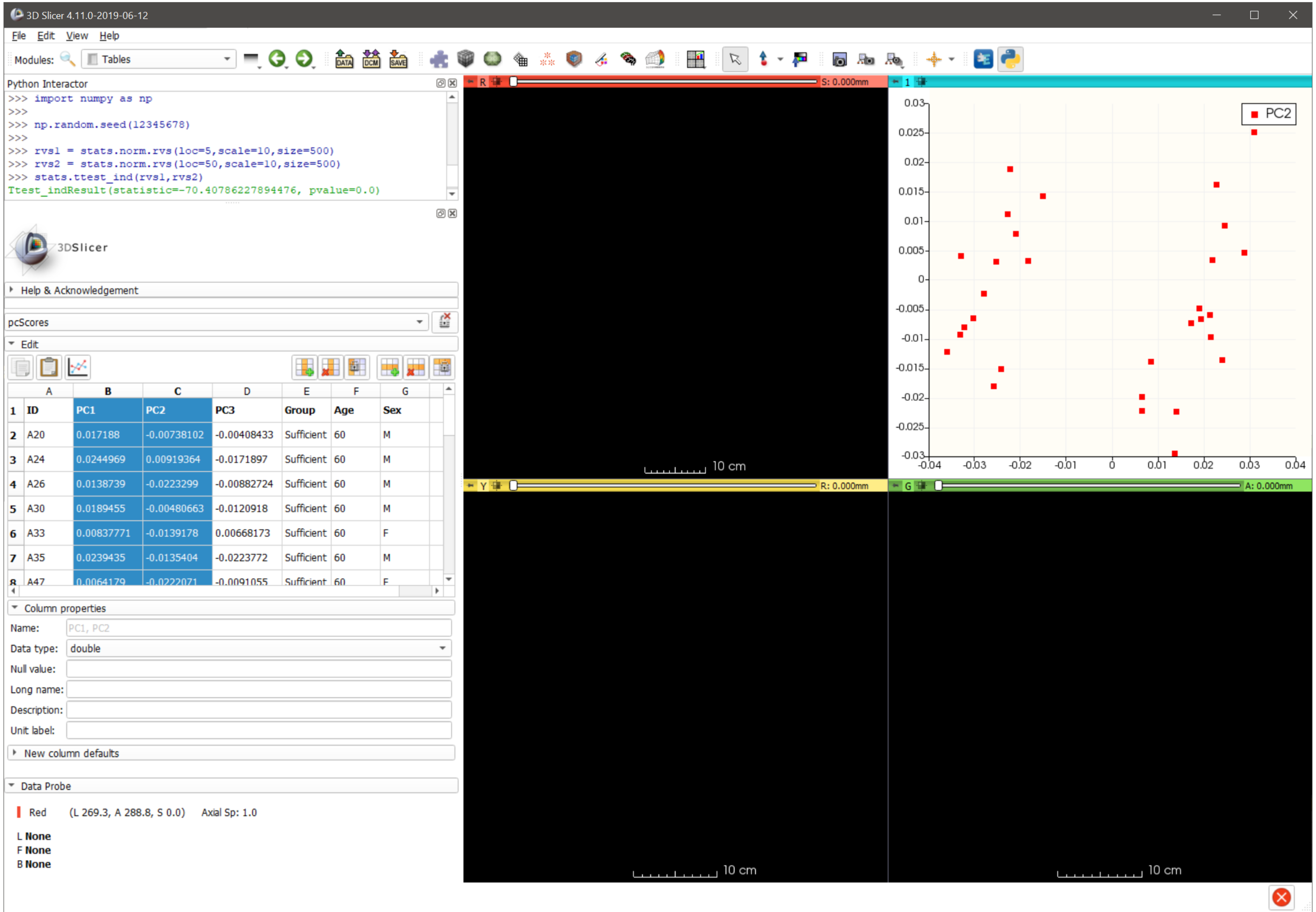
Annotations (Landmarks, Lines, Angles, Curves, Planes)





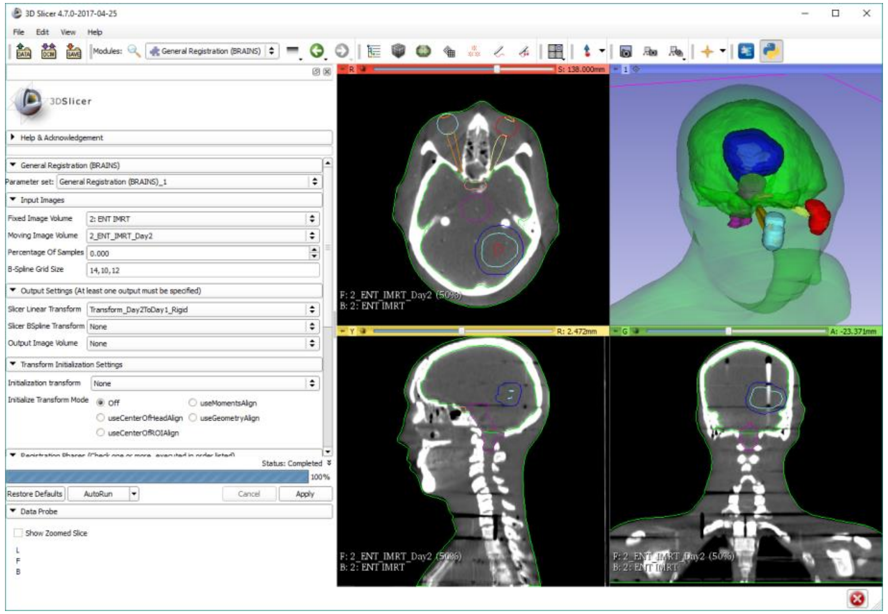


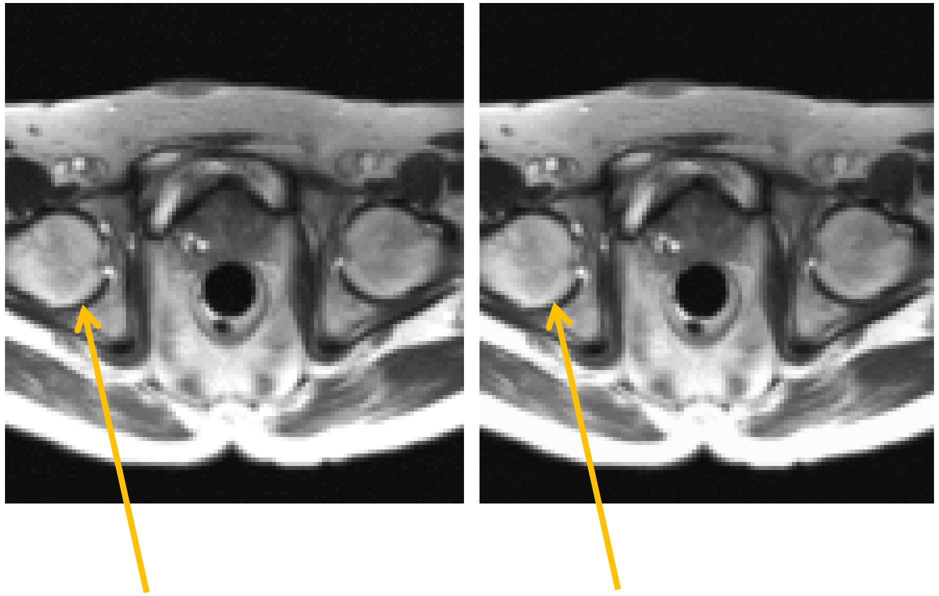
Data Tables, Plots, and statistics (w/ Python)



Registration

- Manual: translation, rotation in 3D
- Automatic: rigid, deformable, with various similarity metrics, initialization methods, optimizers, masking, etc.
- Extensions: structure-based registration, Elastix, etc.

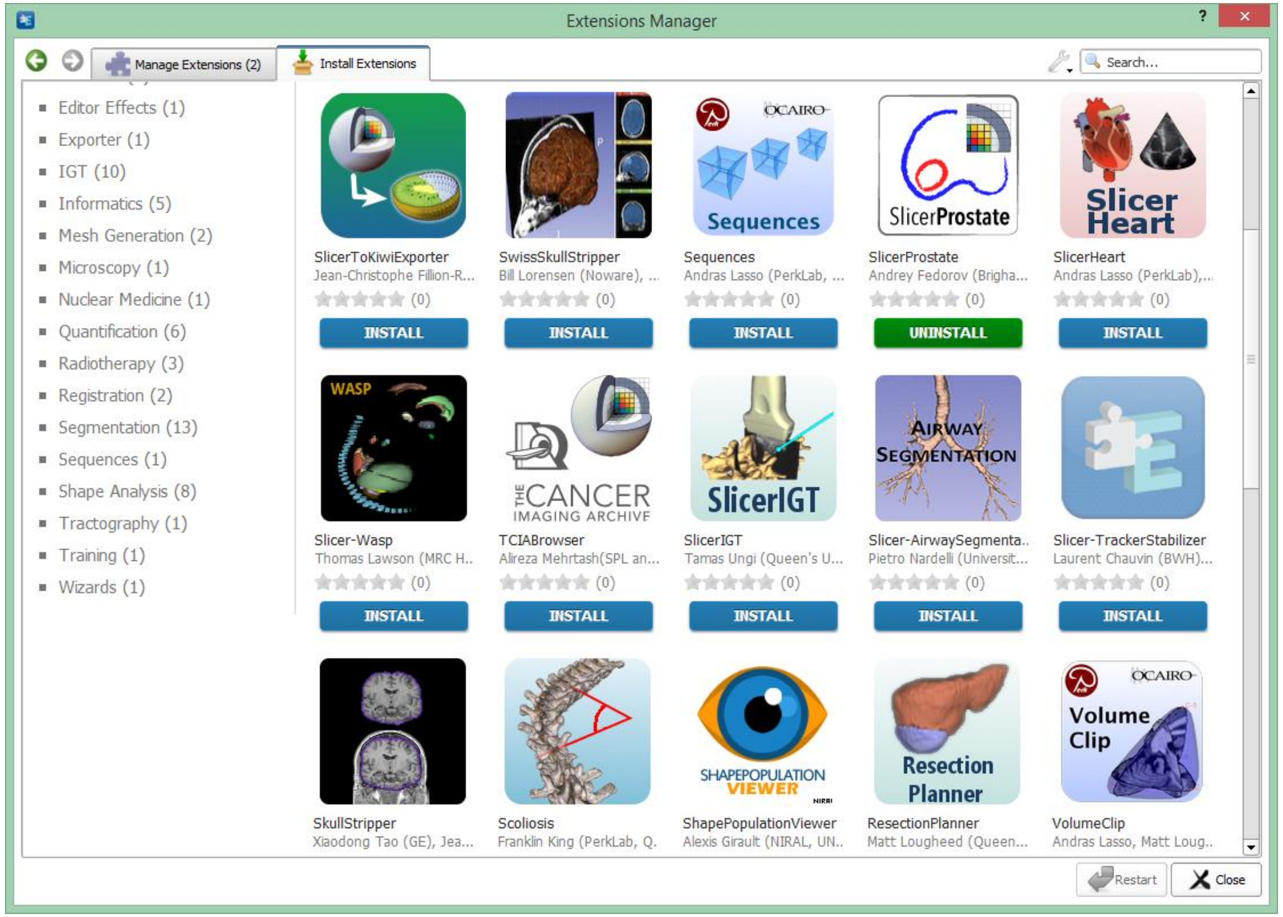




What’s inside Slicer?

- **Slicer core**: Slicer GUI, I/O, visualization and developer interfaces
- **Slicer modules**: internal plugins that depend on the slicer core
- **Slicer extensions**: external plugins installed on demand by the user

Slicer is extensible



The Slicer Extension Manager offers the possibility to the user to download and install additional Slicer modules

Data handling: the MRML scene

- **MRML:** Medical Reality Modeling Language
- All objects (volumetric images, surface models, transforms, etc.) are stored in a hierarchical structure of MRML nodes
- Each MRML node has its own list of custom attributes that can be used to specify additional characteristics for the data object
- Enables the modules to have access to the MRML tree, allowing new extensions to leverage existing processing and visualization functions without directly interfering with other modules

Python in Slicer

The Python console of Slicer gives access to

- Scene objects (MRML)
- Data arrays (volumes, models)
- GUI elements (Qt) that can be encapsulated in a module
- Processing Libraries (more can be installed)
  - numpy
  - VTK
  - ITK
  - CTK

Open Source vs Proprietary software

- **Open source** is a pay-forward model:

You get free access to tens of thousands of manhours already paid and committed by people with no strings attached.

Any new contribution you make it personally or pay for it (with private contracts) will benefit the future users.

Allows free exchange of ideas and data

- **Proprietary software**

Pay now for the features that are already developed.

Pay in future for the new features you asked for it (a.k.a upgrades)

Benefit of open-source development

- In the event of loss of funding, or the developer losing interest (or the ability) in maintaining the software, there is nothing for community to keep the software up-to-date (or even available as-is because of technology changes).
- In open-source model, even if the core development group loose funding, disband or change focus, the community have access the full source code and any one else can pick up the development or maintain as it is in perpetuity.
- It is particularly appealing for publicly funded projects.

But Slicer doesn't work with my datasets!!!

- On 64-bit Oses, Slicer **is only limited by the hardware capabilities of your system**:

However:

- All operations in Slicer are done **in-memory**. I.e., you need to have more quite a bit more memory than your dataset (more on this later). You can address this in two ways:
    1. Buy as much memory as your H/W will support (typically 64-128GB for i7 processors)
    2. Increase the virtual memory on your computer (everything will work but will be quite slow).

- **For 3D rendering**, you need to have GPU that's capable of displaying large 3D texture dimensions and have lots of GPU memory (e.g., TITAN RTX will load datasets up to 24GB). A **2080TI** (about 1/3rd of price of TITAN) is more than sufficient for most datasets.

- **Datasets are sacrosanct**, Slicer will NOT do anything to your data until you tell it to do explicitly

How big of a dataset I can work on with Slicer?

- Depends on what you want to do:
- Rule of thumb 6-10X more RAM than your dataset size.
  - E.g. 1024x1024x1024 scan with intensity ranges from 0-4096 would be 2GB when loaded
  - Depending on the type of the action, RAM requirement would be 4-20GB.
  - Most filters and tasks Slicer is multi-threaded, thus would benefit from multi-core computer architecture
  - If you do registration, requirements would approximately double.
- 3D Volume Rendering (Raycasting) needs a high-end GPU with more memory than your largest dataset.
  - So, example above would work on a GPU with 3GB GPU RAM.
  - It also depends on your GPUs OpenGL hardware capabilities (check https://opengl.gpuinfo.org/)
  - CPU rendering always works, but usually slow (unless you have dozens of cores).
- You can use downsample or crop your volume to match it to your hardware.
- Keep your data as a 3D volume. Reading one large files is faster compared to reading thousands of small files.
- NVME SSDs are very good investments.

Take Home Message

SLICER**MORPH** is not a traditional research project, but a chance to build a digital community of organismal biologists and quantitative morphologists around 3D Slicer that value open science and collaboration.

We are looking forward to your engagement.

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Extended SlicerMorph Team

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Slicer Developer Community

SLICERMORPH

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