Agency for Science, Technology and Research
SINGAPORE

Rapid prototyping of medical image analytics used in clinical decision support systems

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Agenda

- Introduction – About SBIC, Nature of work
- Development of Research tools
  - Challenges
  - Tools used
  - Benefits
- Use cases
  - Research studies
  - Clinical trials
  - Clinical translation
- Takeaways/Conclusion

Singapore Bioimaging Consortium – IMAGING TODAY THE MEDICINE OF TOMORROW

CREATING GROWTH, ENHANCING LIVES

Molecules → Animals → Man

BIOIMAGING

Biologists

Chemists

Engineers

Physicists

Clinicians

An Integrated multidisciplinary imaging platform











- Lab of Bio-optical Imaging
- Lab of Metabolic Medicine
- Lab of Molecular Chemistry
- Lab of Isotopic Molecular Imaging
- Translational Cardiovascular Imaging
- Signal and Image Processing
- Metabolic Imaging
- MR Methods Development
- Neuroscience Cluster
- Fat Metabolism & Stem cell

Research

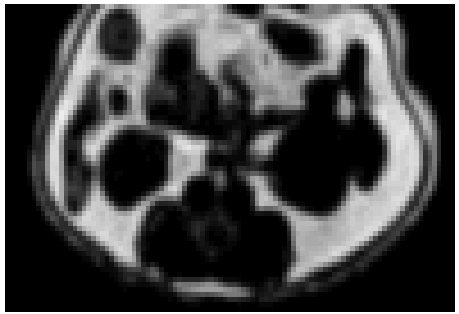
Neuroscience	Obesity & Diabetes
Cancer	Skin
Metabolism	Woman health
Stem cell	Food Quality
Cardiovascular	Optics

Need Statement : SBIC – A Bioimaging Institute

SBIC is place on earth for every Image & Data Analytics enthusiast

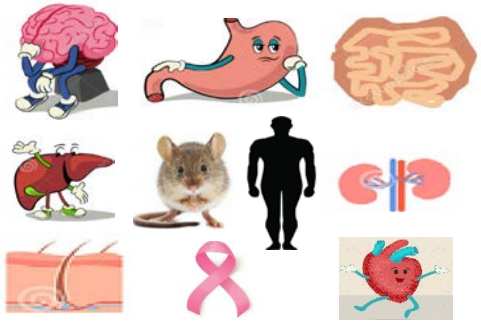
Multimodal Images

Optical, CT, MR; Cells, tissues; organs; structural, functional



Spectrum of research

liver, brain, abdomen, cardiac ; cancer, metabolism, neuro



Research & Clinical tools

Variability in data, limited data, user interaction; Specific to need

Image Reconstruction ;
Image Denoising;
Artifact Reduction;
Super resolution
Research Tools

Big data analytics;
Inverse problems;
Signal processing;
Live cell analysis

Multimodal Data Analytics
Decision Support systems
Atlas based analysis
Mathematical Modelling

Advanced Image analysis & Deep Learning

.....

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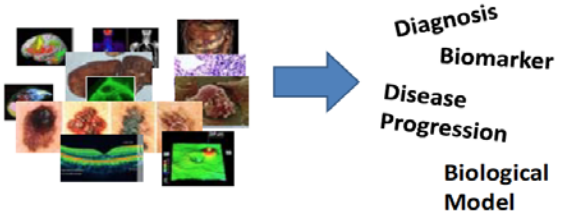
Why we need Imaging & Image Processing ?

Medical imaging is the process of using technology to view in vivo for

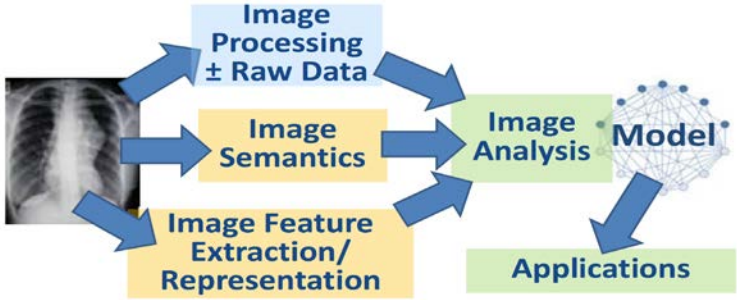
- *Structural & functional understanding*
- *Diagnosis & monitoring, and*
- *treating medical problems.*



Most medical imaging data is Qualitative in nature

Images → *Understanding*

Qualitative analysis → *Quantitative information*



Improved visualization ;
High resolution;
in-vivo understanding;
enhanced detection ; interpretation, diagnosis etc.

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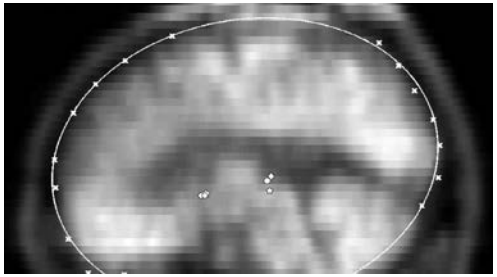
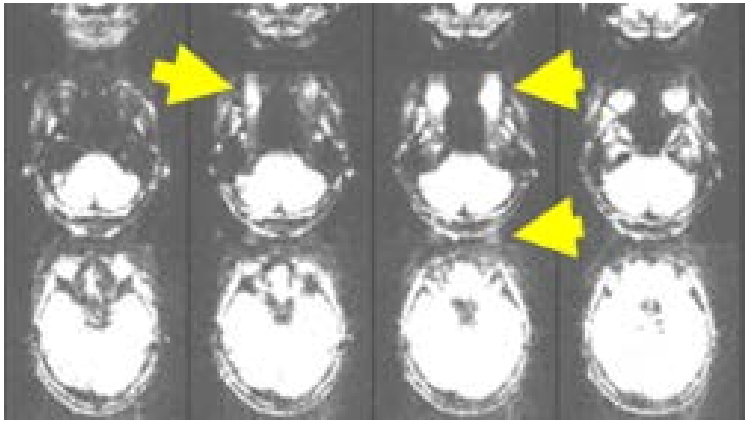
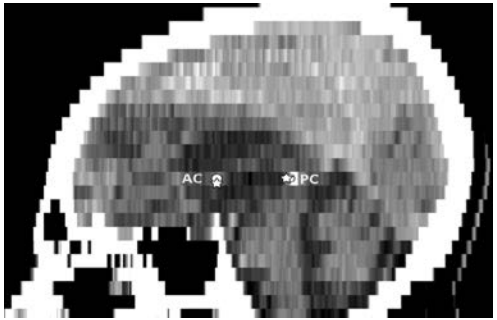
Challenges

Quality of Acquisitions – Garbage in ; Garbage out



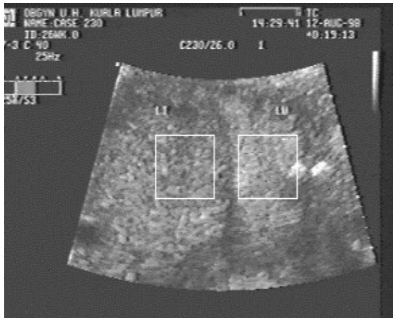
Limitations in Scanner settings



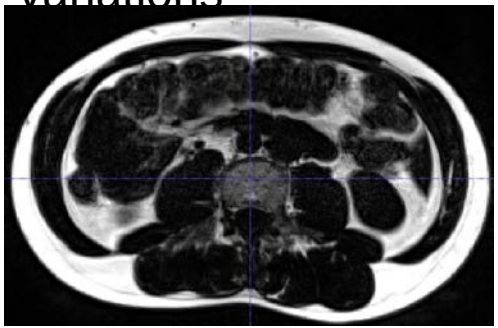


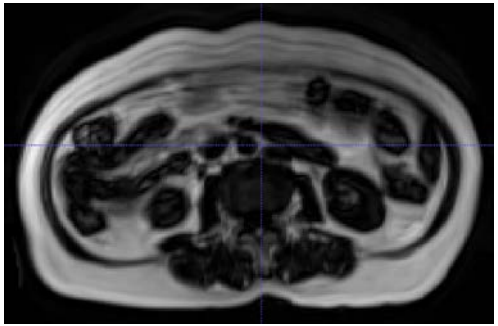
Acquisition Variations

Anatomical Variations



Motion Artifacts





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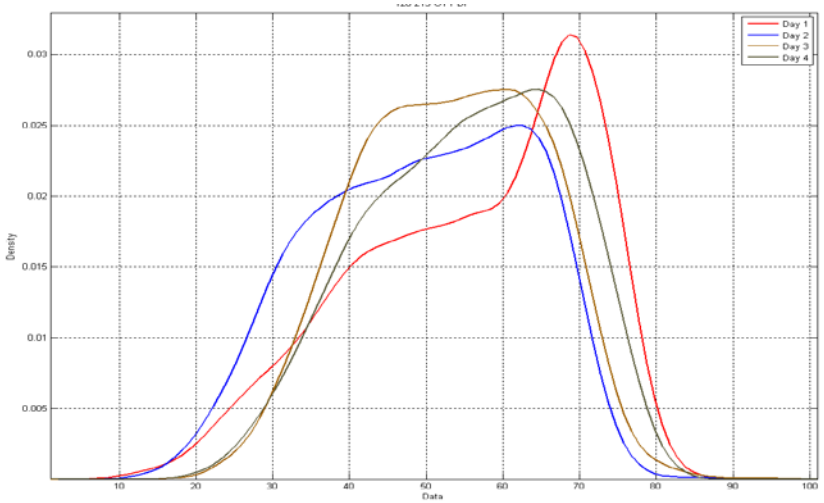
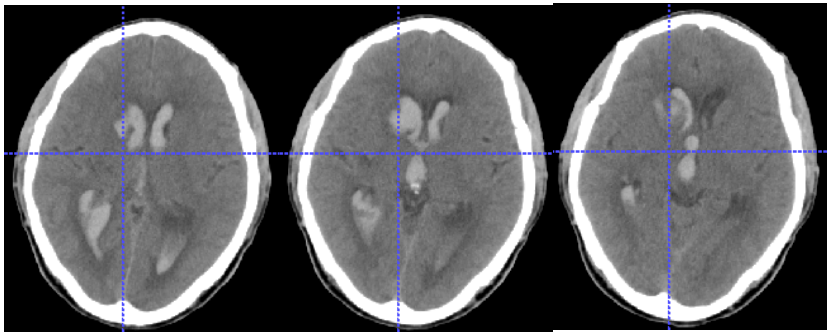
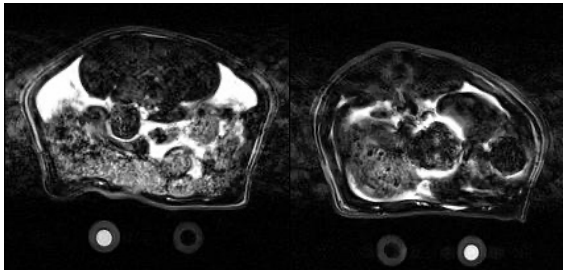
Practical issues

- Data from different hospitals
- Multiple scanners – Siemens, GE, Toshiba, Philips
- Different scan settings
- Varying slice thickness 2.5mm – 8mm
- Varying window settings
- Variability in ground truth
- Variability in Blood HU
- Artifacts and Noise
- Head tilt

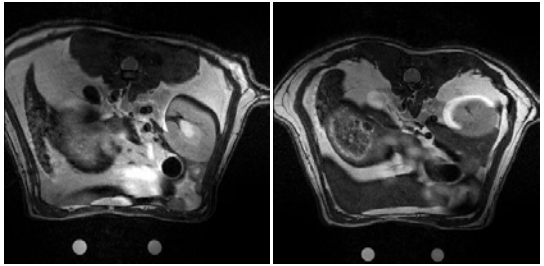




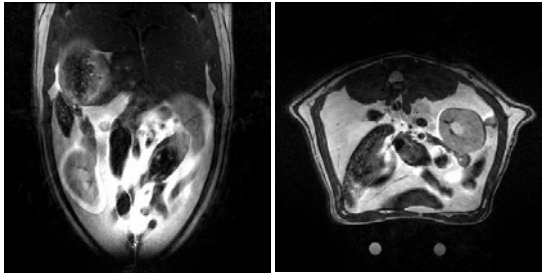
Some real-life examples - Continued



Pre- & Post- intervention scan

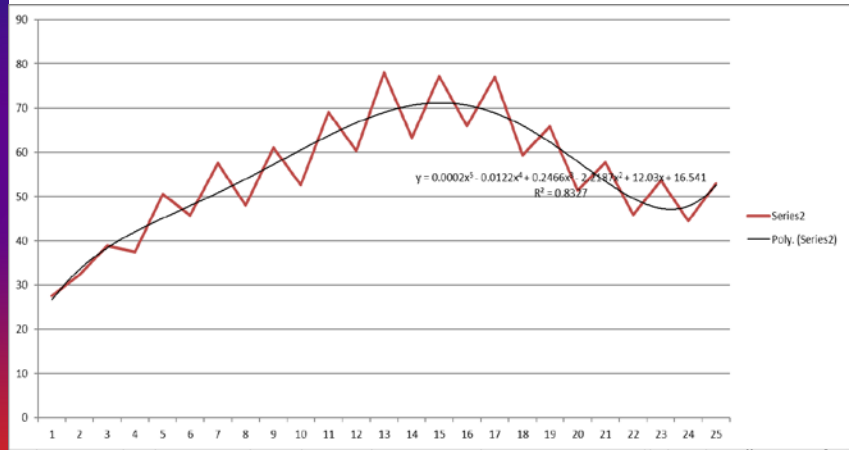


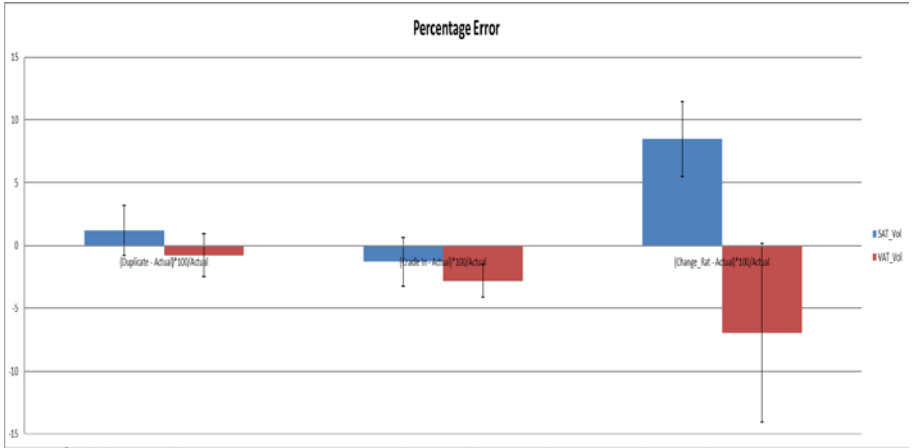
Wrong field of view, Chemical shift artefacts



Bias field artefacts, Improper water suppression

Improper placement & taping, Water suppression not activated , phase swaps Motion compensation not in place etc.





Bhanu Prakash KN, Venkatesh Gopalan, Swee Shean Lee, S. Sendhil Velan ."Quantification of Abdominal Fat Depots in Rats and Mice during Obesity and Weight Loss Interventions". Published: October 13, 2014, https://doi.org/10.1371/journal.pone.0108979

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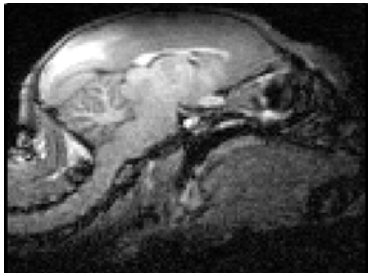
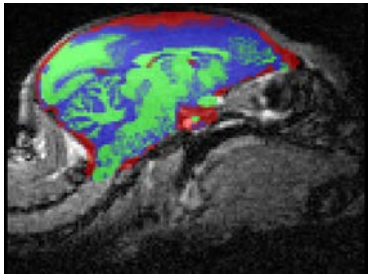
Bias-field spoils segmentation

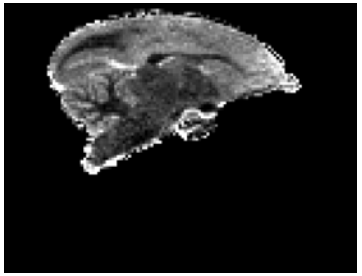
MPRAGE signal inhomogeneity from surface coil

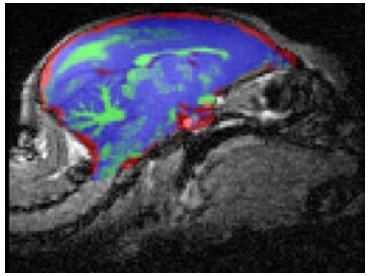




Poor segmentation

Add MP2RAGE-T1 with no signal inhomogeneity





Improved segmentation

Acknowledgment: Isaac Huen, PhD, SBIC

Lum, FM., Zhang, W., Lim, KC. Isaac Huen, Bhanu Prakash KN *et al.* Multimodal assessments of Zika virus immune pathophysiological responses in marmosets. *Sci Rep* **8,** 17125 (2018). https://doi.org/10.1038/s41598-018-35481-6

Image based pain points

- ML or DL needs painful, time-consuming, & expensive data annotation
- Multiple blinded annotations of different types
- Domain expertise

Radiologists Already Overloaded

- Data sets could be – long videos (Colonoscopy) – Marking of polyps
- Very small structures – Knee cartilage ; Gastric cancer wall thickening
- 4D & Longitudinal data sets – Cardiac, Treatment phase, Clinical trials
- Limited data sets – Rare conditions

Time, Errors, Variability, Cost

- Access to data
- Right tools for Annotation & exporting
- Combining Multimodal unstructured data; Text & Images
- Missing information ; Causality etc.

Scalability, Tool development

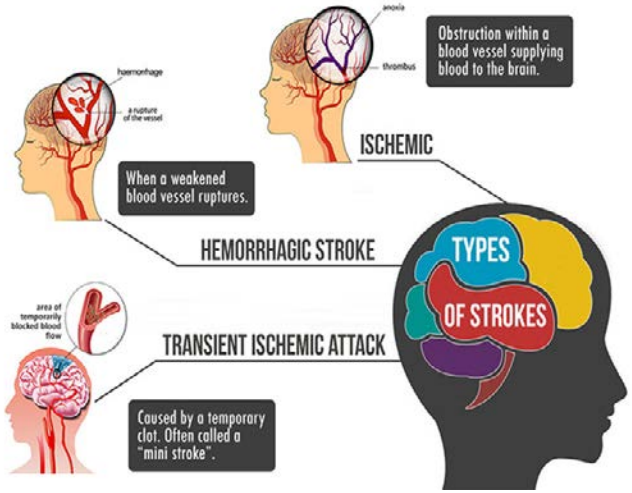
Stroke Suite Roadmap

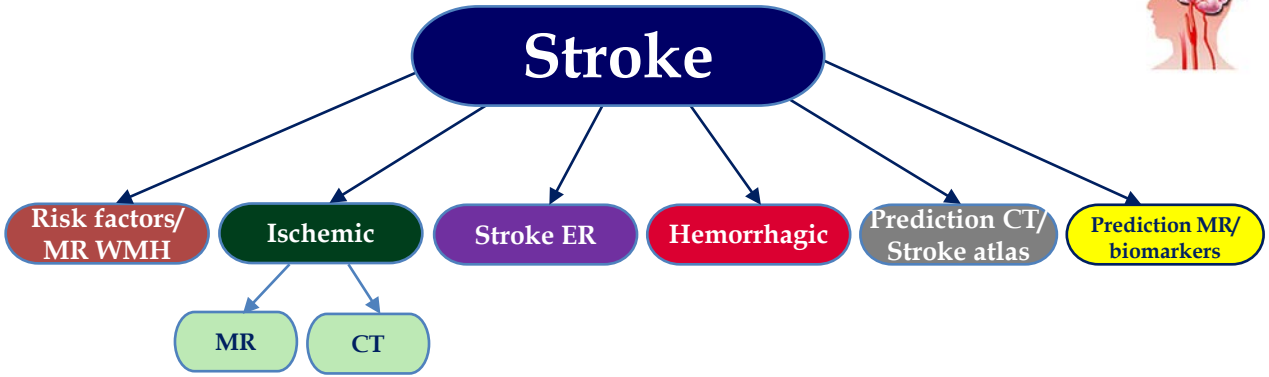
Stroke is the No. 1 cause of adult disability

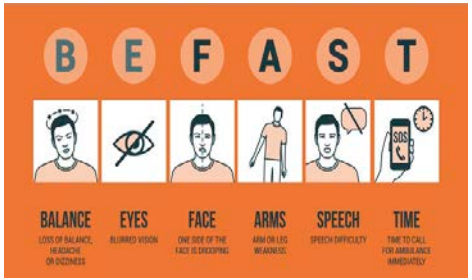
High mortality, morbidity, social & economical burden

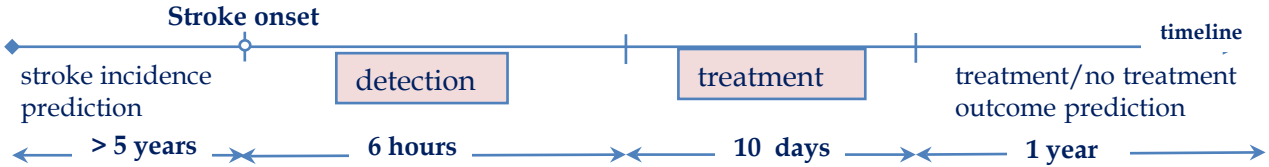
Time critical to treat

2 million brain cells die per minute









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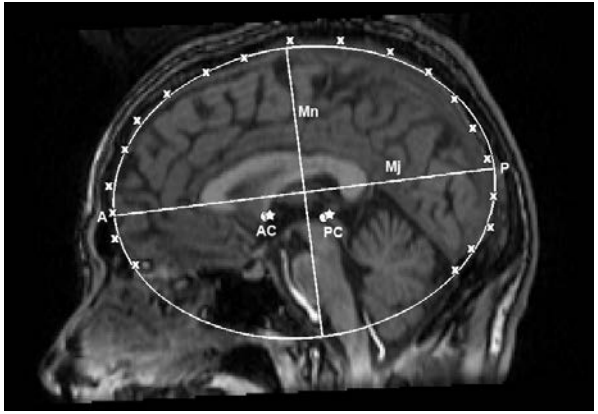
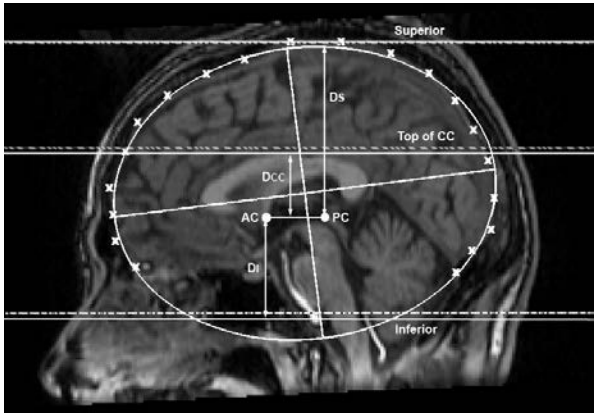
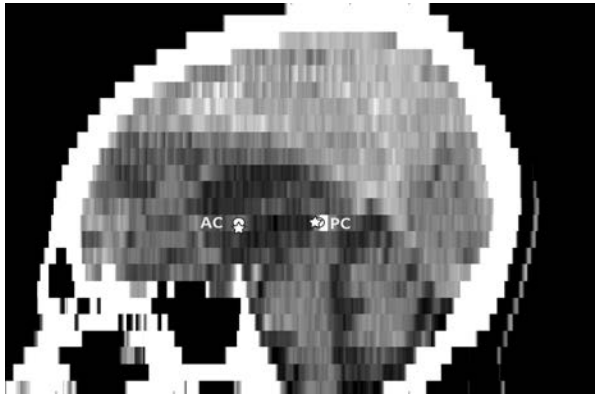
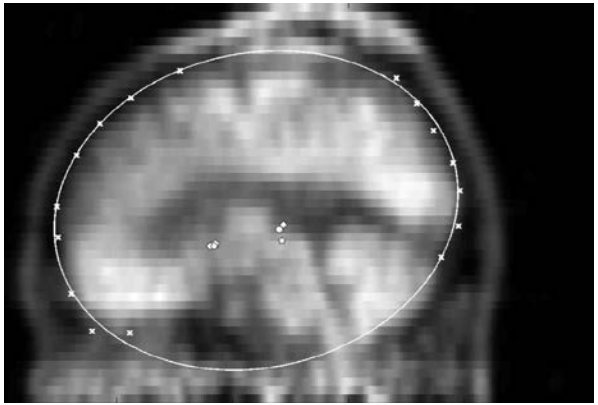
Landmark calculation based on ellipse fitting







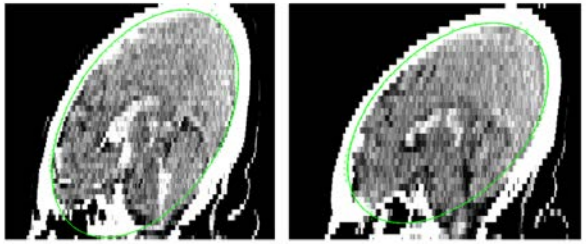


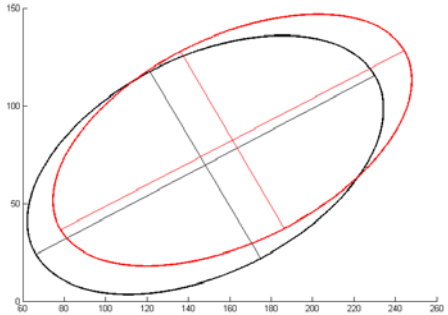
Curve Fitting
Fuzzy Logic
GUI Layout
Global Optimization
Image Processing
MATLAB Compiler
Optimization
Partial Differential Equation
Signal Processing
Statistical Parametric
Statistics & Machine Learning
Symbolic Math Toolbox

Volkau I, Puspitsari F, Nowinski WL: *A simple and fast method of 3D registration and statistical landmark localization for sparse multi-modal/time-series neuroimages based on cortex ellipse fitting*. The Neuroradiology Journal 2012;25(1):98-111.
Volkau I, Bhanu Prakash KN, Ng TT, Gupta V, Nowinski WL: *Localization of brain landmarks such as the anterior and posterior commissures based on geometrical fitting.* US patent no. US8,045,775 granted on 25 Oct 2011.

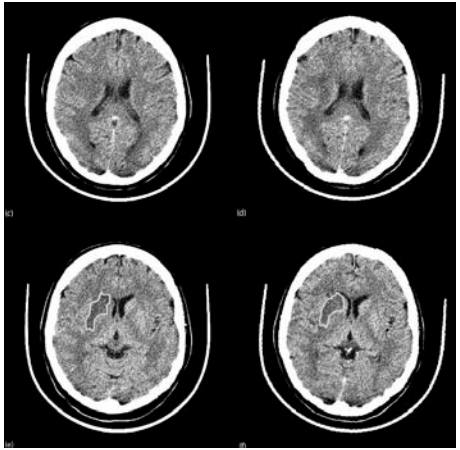
Registration of atlas, sparse data & time series based on ellipse fitting - Low computation / fast

Hemorrhage: days 3 and 4

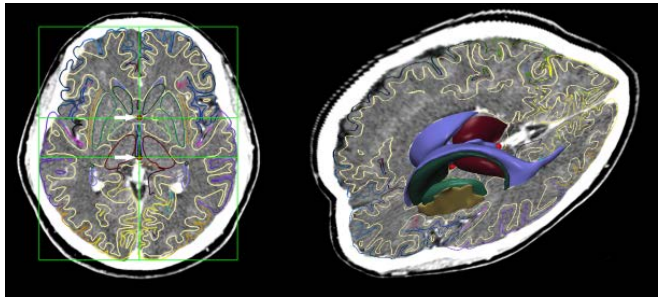




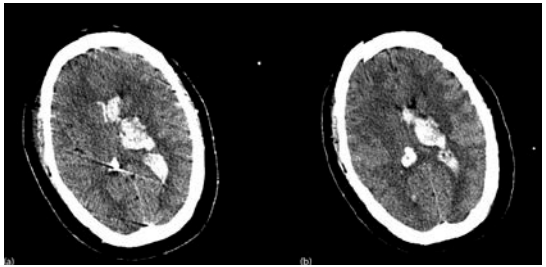
Ischemic stroke: days 1 and 6



Atlas-scan registration



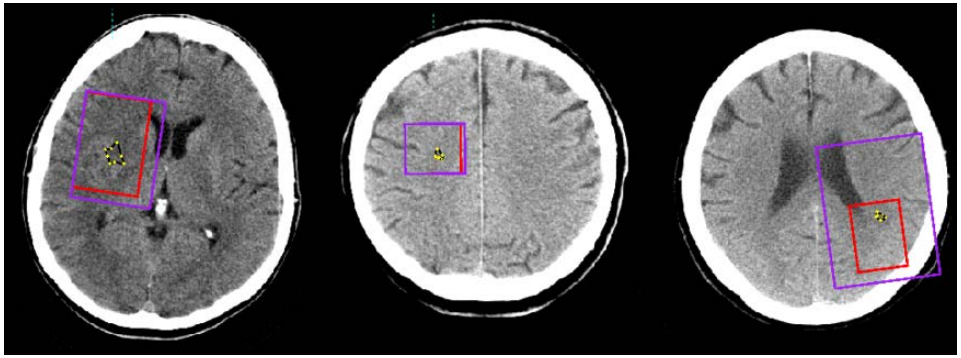
Helps Quantification
Understanding changes
Supports decision making
Robust, Accurate & efficient
Eliminates user bias
Manhours saved

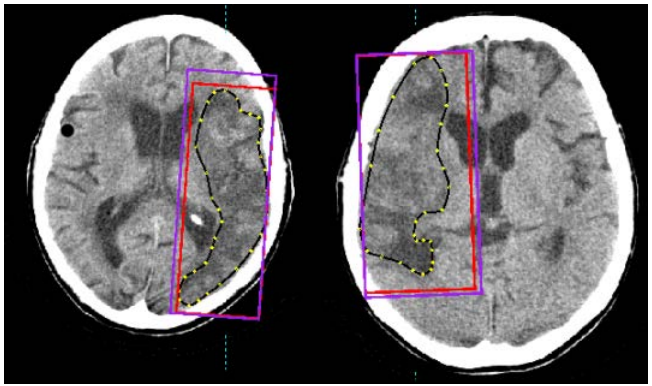


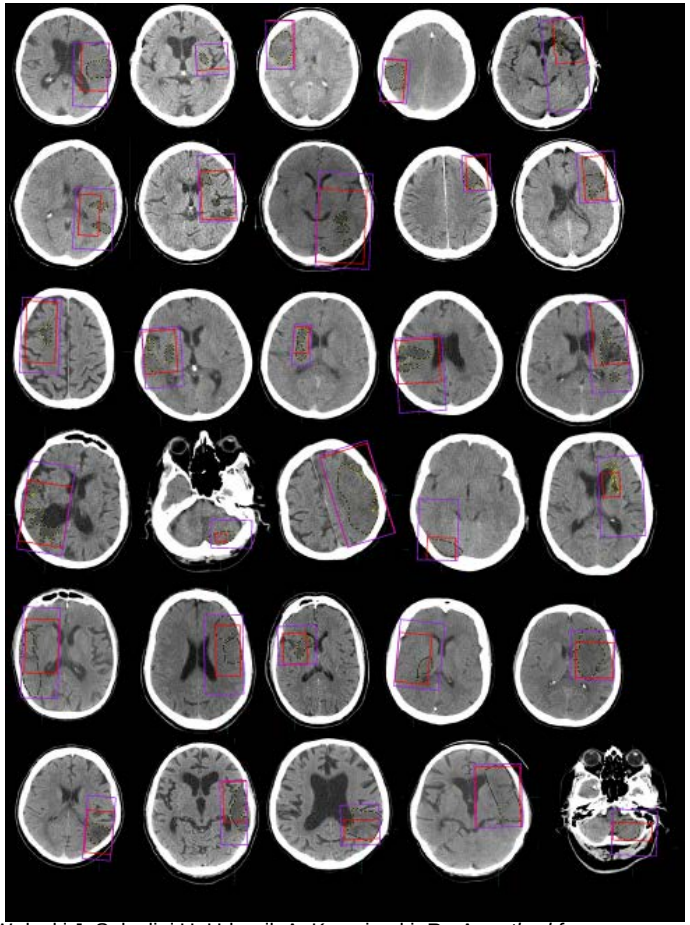
Volkau I, Puspitsari F, Nowinski WL: A simple and fast method of 3D registration and statistical landmark localization for sparse multi-modal/time-series neuroimages based on cortex ellipse fitting. The Neuroradiology Journal 2012;25(1):98-111.

Volkau I, Bhanu Prakash KN, Ng TT, Gupta V, Nowinski WL: Localization of brain landmarks such as the anterior and posterior commissures based on geometrical fitting. US patent no. US8,045,775 granted on 25 Oct 2011.

Stroke detection / localization on NCCT



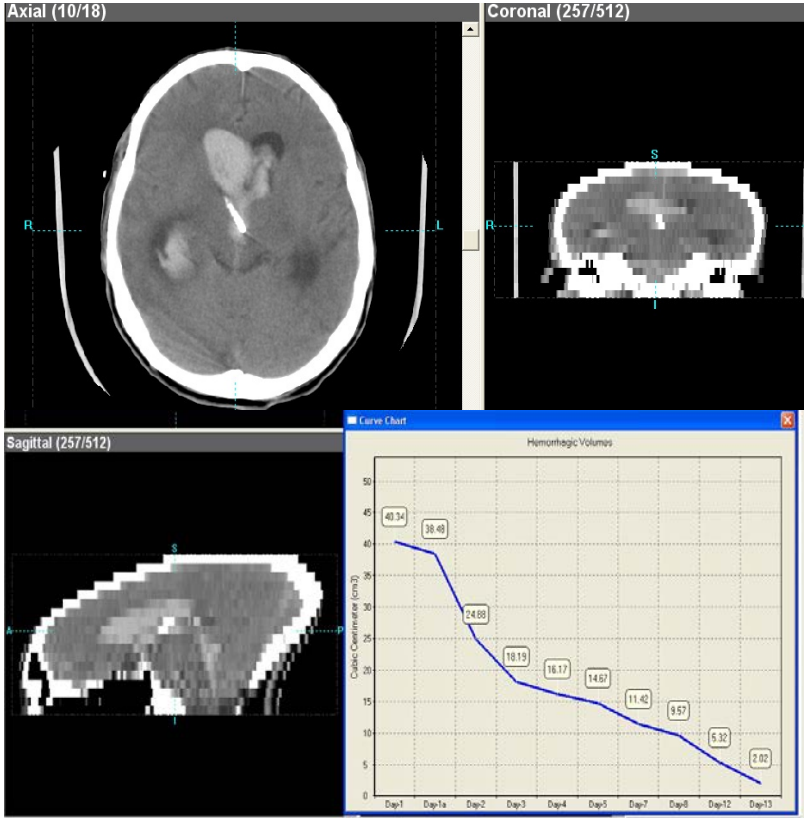


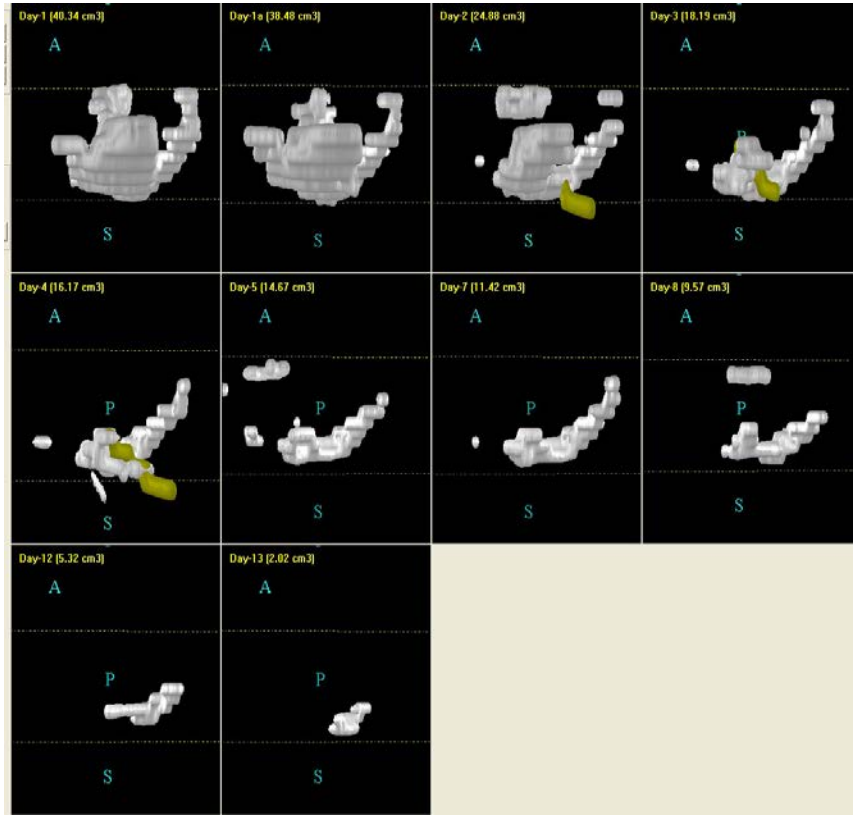


Improved detection, Time efficient, Accurate

Nowinski WL, Gupta V, Qian GY, He J, Ambrosius W, Chrzan RM, Polonara G, Mazzoni C, Mol M, Salvolini L, Walecki J, Salvolini U, Urbanik A, Kazmierski R: A *method for automatic detection, localization and volume estimation of ischemic infarcts in unenhanced Computed Tomography scans*. Stroke (submitted).

Hemorrhage stroke quantification & tracking



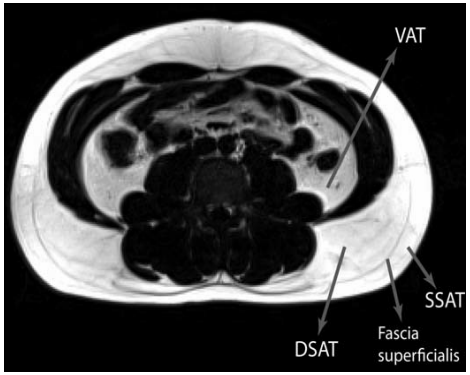


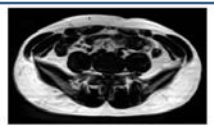
Bhanu Prakash KN, Nowinski WL: *Method and system of segmenting CT scan data*. Patent pending US61/033105 provisional application filed on 3 Mar. 2008.

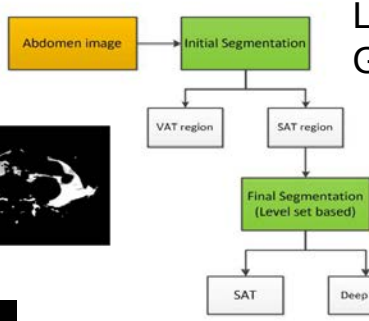
Bhanu Prakash KN, Morgan TC, Hanley DF, Nowinski WL: *A brain parenchyma model-based segmentation of intraventricular and intracerebral haemorrhage in CT scans*. The Neuroradiology Journal 2012 Bhanu Prakash KN, Hu J, Morgan T, Hanley DM, Nowinski WL: *Comparison of three segmentation techniques for intra-ventricular and intra-cerebral haemorrhages in unenhanced CT scans*. Journal of Computer Assisted Tomography 2012;36(1):109-20.

Fat Analysis tools in Rodents and Humans

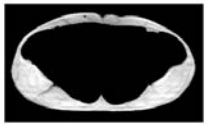
- Adiposity levels associated with risk of metabolic diseases.
- Physiologic effects based on anatomical location.
- Abdomen:
  - *Visceral Adipose Tissue (VAT)*
  - *Subcutaneous Adipose Tissue (SAT)*
    - *Superficial SAT*
    - *Deep SAT*
    - *Separated by Fascia Superficialis*



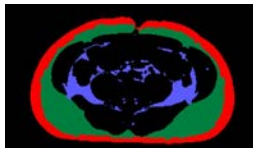




Level sets &
Graph cut methods



Final segmentation



Human Abdominal fat compartments

Original Research | Free Access

Automated segmentation of visceral and subcutaneous (deep and superficial) adipose tissues in normal and overweight men

Suresh Anand Sadananthan PhD, Bhanu Prakash KN, PhD ... See all authors

First published: 07 May 2014 | https://doi.org/10.1002/jmri.24655 | Citations: 36

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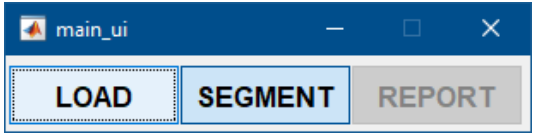
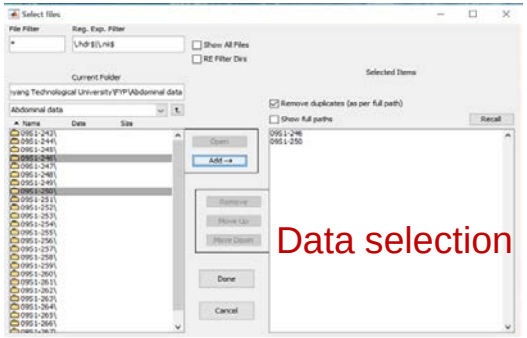
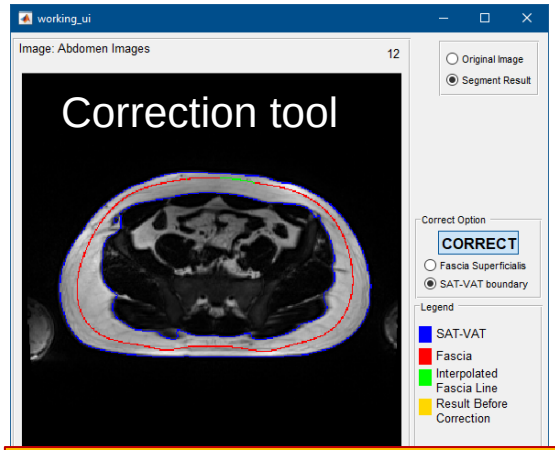
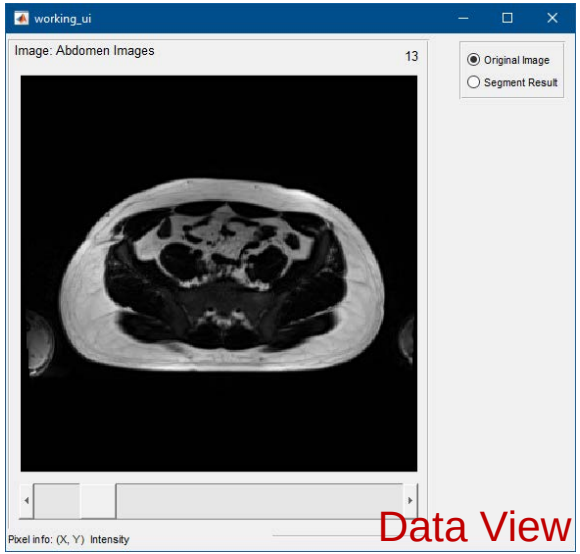
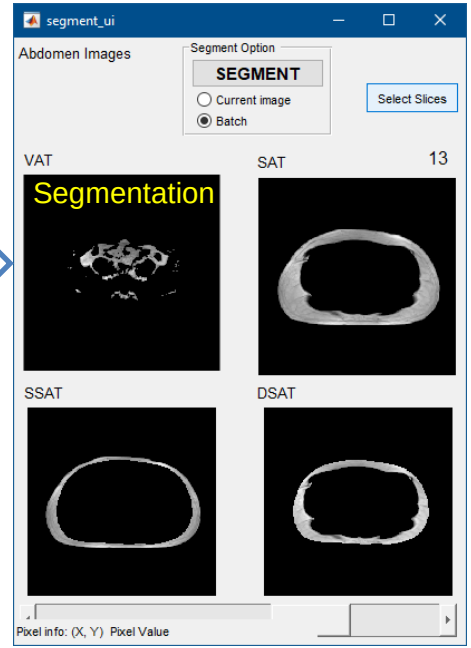
Framework developed in MATLAB – saved manhours ~ 1000 hours

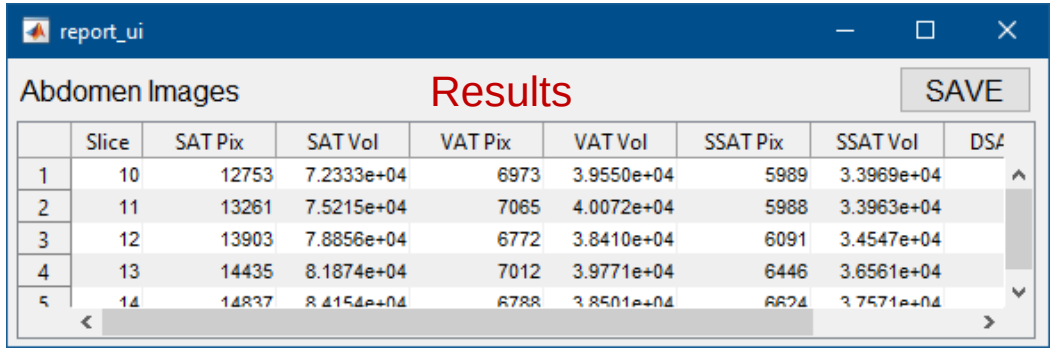












	Slice	SAT Pix	SAT Vol	VAT Pix	VAT Vol	SSAT Pix	SSAT Vol	DSA
1	10	12753	7.2333e+04	6973	3.9550e+04	5989	3.3969e+04	
2	11	13261	7.5215e+04	7065	4.0072e+04	5988	3.3963e+04	
3	12	13903	7.8856e+04	6772	3.8410e+04	6091	3.4547e+04	
4	13	14435	8.1874e+04	7012	3.9771e+04	6446	3.6561e+04	
5	14	14837	8.4154e+04	6788	3.8501e+04	6624	3.7571e+04	

Man hours saved > 1000 hrs

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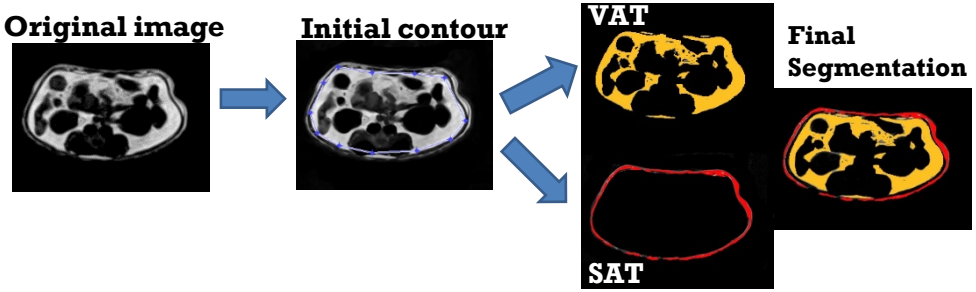
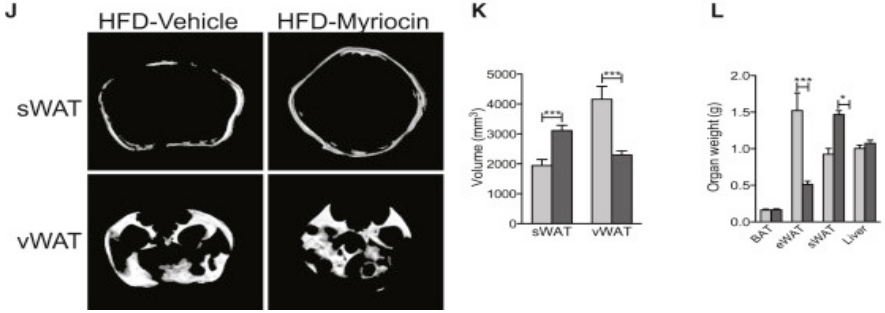
MATLAB based Rodent Fat Analysis tool





Cell Metabolism

Volume 24, Issue 6, 13 December 2016, Pages 820-834

CellPress

Article

Adipocyte Ceramides Regulate Subcutaneous Adipose Browning, Inflammation, and Metabolism

Bhagirath Chaurasia [1, 14, 15, 16], Vincent Andre Kaddai [1, 14], Graeme Iain Lancaster [1], Darren C. Henstridge [2], Sandhya Sriram [3], Dwight Lark Anolin Galam [4], Venkatesh Gopalan [5], K.N. Bhanu Prakash [5], S. Sendhil Velan [5], Sarada Bulchand [6], Teh Jing Tsong [7], Mei Wang [7], Monowarul Mobin Siddique [8], Guan Yuguang [4], Kristmundur Sigmundsson [4], Natalie A. Mellet [9], Jacquelyn M. Weir [9], Peter J. Meikle [9] ... Scott A. Summers [1, 15]

> Biosci Rep. 2021 Jan 12;BSR202017

A 12-week aerobic ex function with lower a high fat diet fed rats

Venkatesh Gopalan [1], Jadegoud Yaliga Sanjay Kumar Verma [1], Suresh Anand S Sendhil Velan [1 2 3]

PLOS ONE

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RESEARCH ARTICLE

Quantification of Abdominal Fat Depots in Rats and Mice during Obesity and Weight Loss Interventions

Bhanu Prakash KN, Venkatesh Gopalan, Swee Shean Lee, S. Sendhil Velan

Preclinical MRI pp 259-268 | Cite as

Rodent Abdominal Adipose Tissue Imaging by MR

Authors Authors and affiliations

Bhanu Prakash KN ✉, Jadegoud Yaligar, Sanjay K. Verma, Venkatesh Gopalan, S. Sendhil Velan

Lipids

Fat Storage-inducing Transmembrane Protein 2 Is Required for Normal Fat Storage in Adipose Tissue *

Diego A. Miranda [‡, 1], Ji-Hyun Kim [‡], Long N. Nguyen [‡], Wang Cheng [§], Bryan C. Tan [‡], Vera J. Goh [‡],

PLOS BIOLOGY

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RESEARCH ARTICLE

Narciclasine attenuates diet-induced obesity by promoting oxidative metabolism in skeletal muscle

Sofi G. Julien ✉, Sun-Yee Kim ✉, Reinhard Brunmeir, Joanna R. Sinnakannu, Xiaojia Ge, Hongyu Li, Wei Ma, Jadegoud Yaligar, Bhanu Prakash KN, Sendhil S. Velan, Pia V. Röder, Qiongyi Zhang, Choon Kiat Sim, [...], Feng Xu ✉

Open Access | Published: 20 May 2016

Effect of Exercise and Calorie Restriction on Tissue Acylcarnitines, Tissue Desaturase Indices, and Fat Accumulation in Diet-Induced Obese Rats

Venkatesh Gopalan, Navin Michael, Seigo Ishino, Swee Shean Lee, Adonsia Yating Yang, K. N. Bhanu Prakash, Jadegoud Yaligar, Suresh Anand Sadananthan, Manami Kaneko, Zhihong Zhou, Yoshinori Satomi, Megumi Hirayama, Hidenori Kamiguchi, Bin Zhu, Takashi Horiguchi, Tomoyuki Nishimoto & S. Sendhil Velan ✉

Scientific Reports 6, Article number: 26445 (2016) | Cite this article

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MATLAB based Rodent abdominal fat segmentation tool

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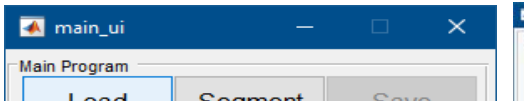
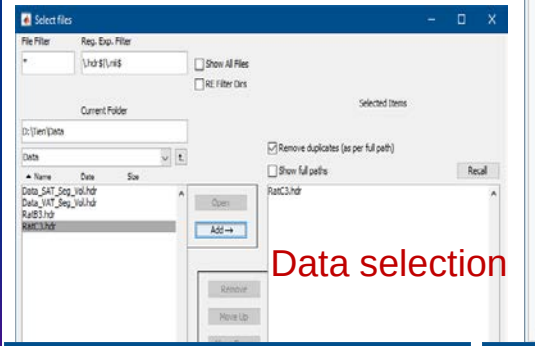
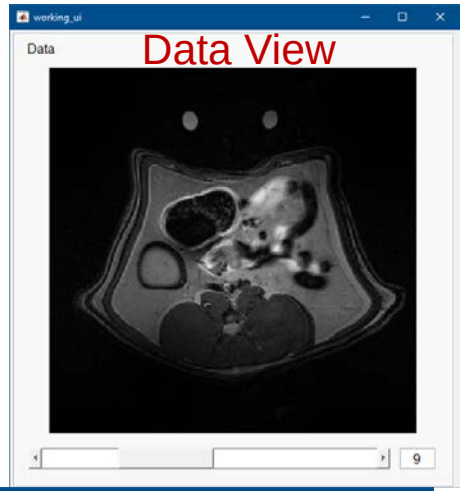
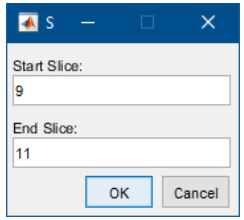
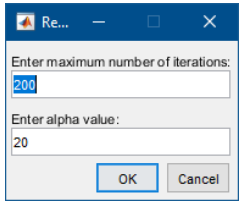
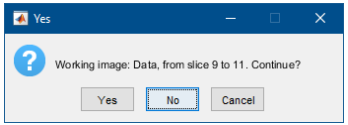




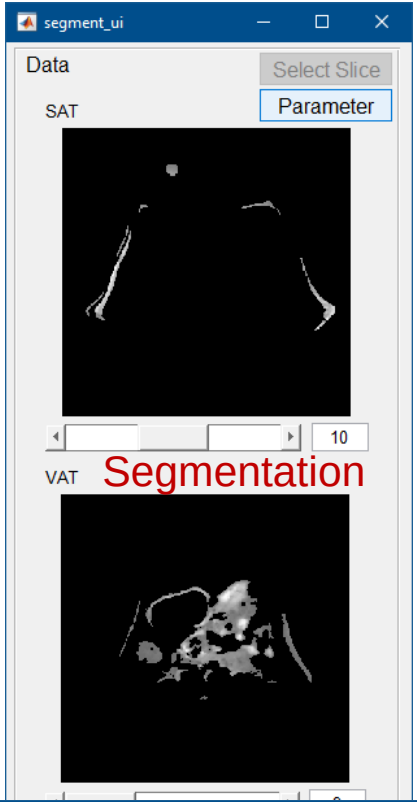


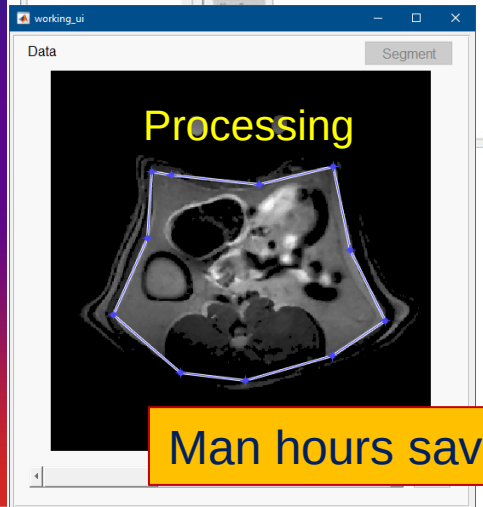


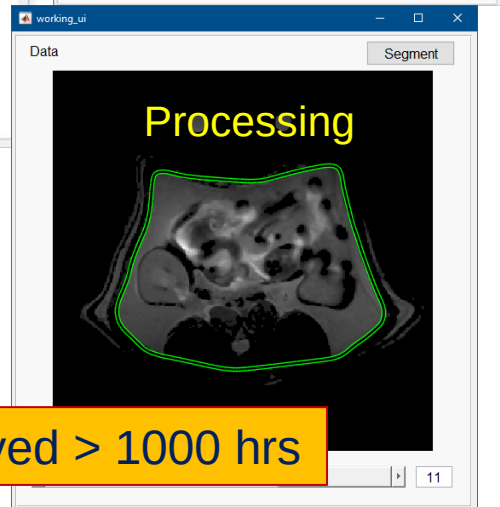




Parameter selection

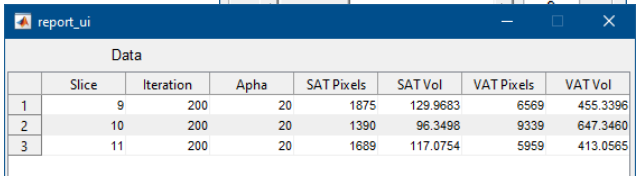






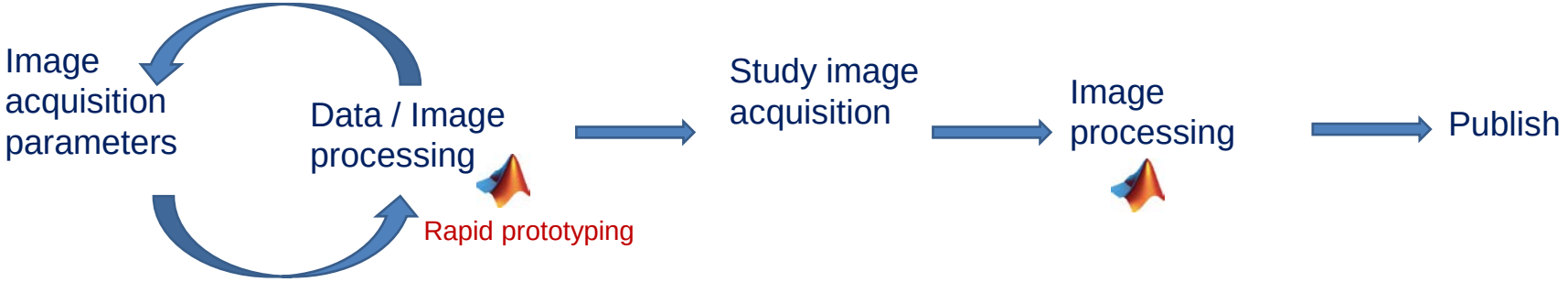
Man hours saved > 1000 hrs

Results



	Slice	Iteration	Apha	SAT Pixels	SAT Vol	VAT Pixels	VAT Vol
1	9	200	20	1875	129.9683	6569	455.3396
2	10	200	20	1390	96.3498	9339	647.3460
3	11	200	20	1689	117.0754	5959	413.0565

Take Home message / Conclusions



Finalizing image processing before starting study has advantages:

- Image quality fit for purpose
- Measured variables, outputs, image processing pipelines are finalized
- Hypotheses can be framed and pre-registered

Disadvantage

- May require manpower and expertise for optimization

Recommendations

- *Have a pilot study*
- *Test / optimize the acquisition together with image processing*

saved manhours, saved cost, improved accuracy, easy to prototype, easy to learn, deployable, …..

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Dr. Ihar Volkov – NTU

Dr. Kuan Jin Lee – SBIC

Johns' Hopkins Hospital – USA

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