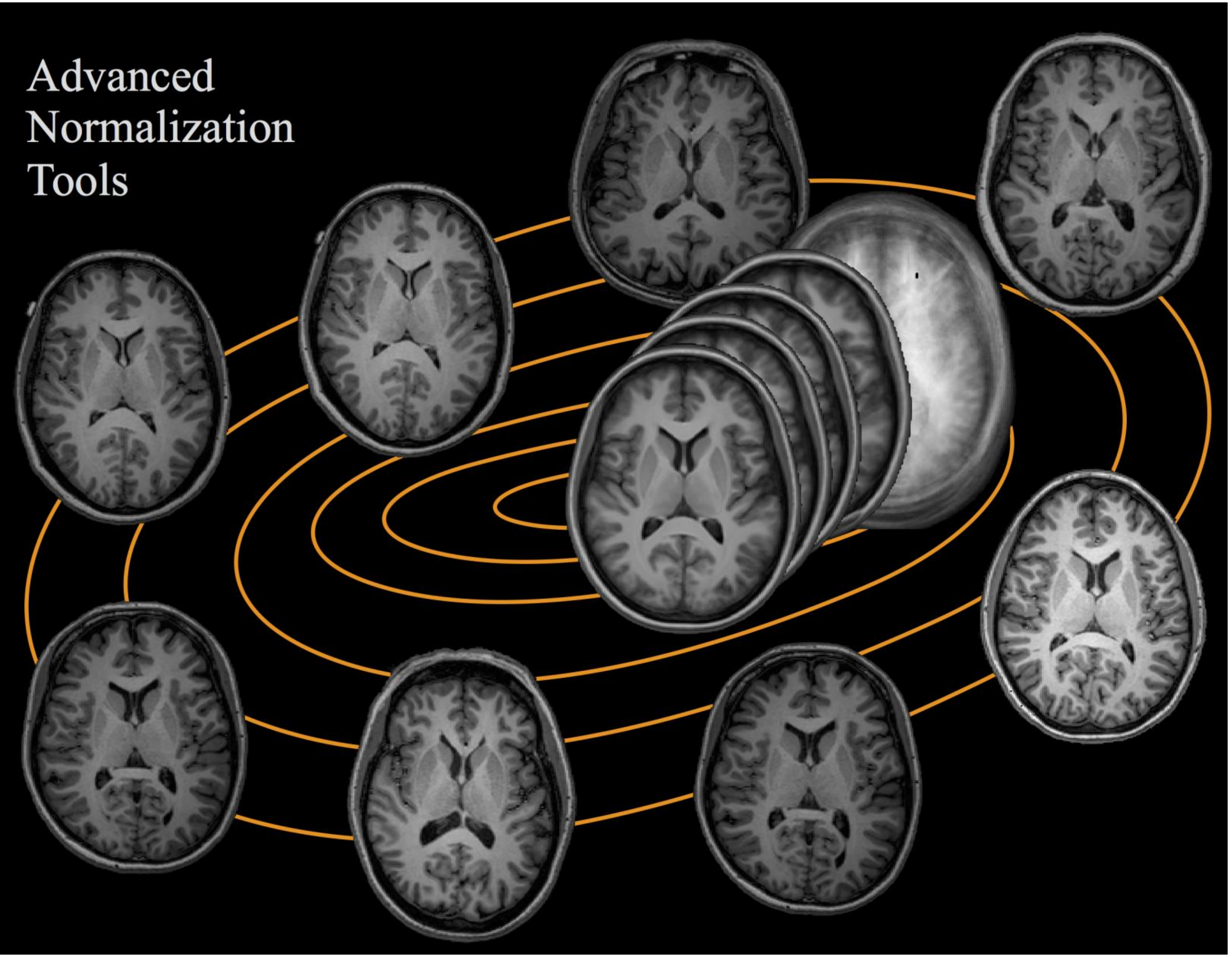


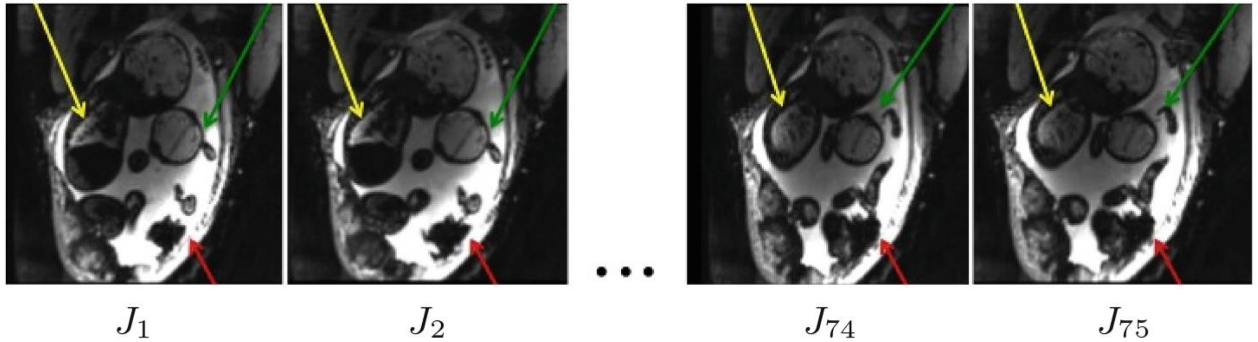
Medical Image Processing by ANTsR

2017/1/9

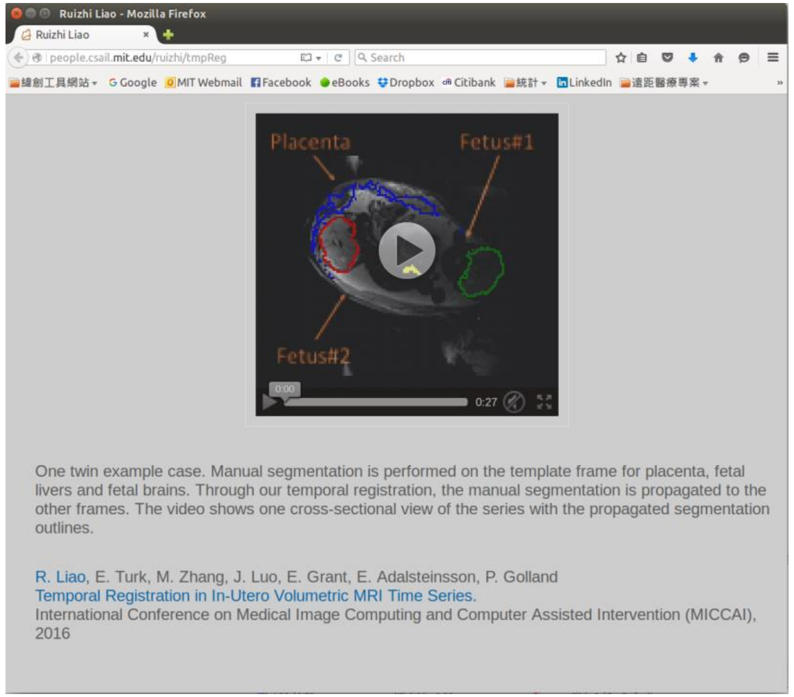
許駿鵬 @ Taipei R User Group

醫療影像處理 – Case

嬰兒胎盤 MRI 影像處理

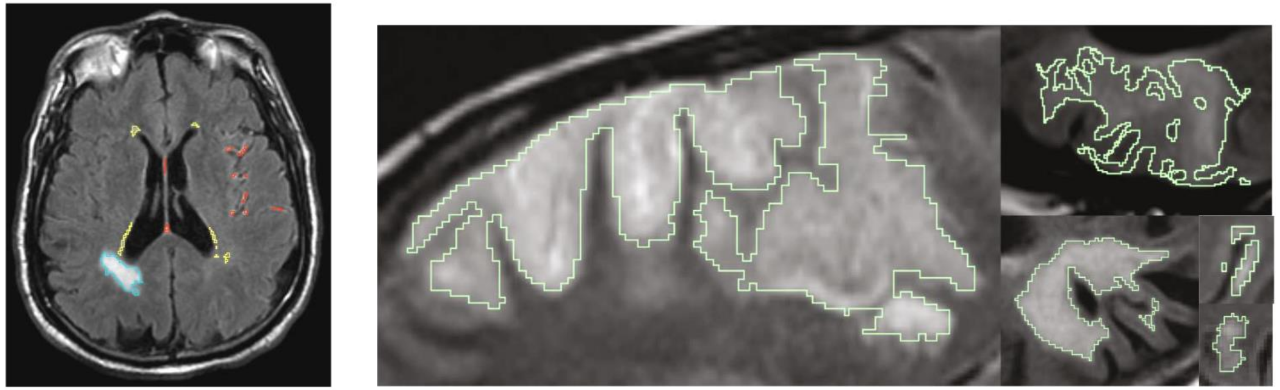


Source : R. Liao, “Temporal Registration in In-Utero Volumetric MRI Time Series.” MICCAI, 2016



[影片連結]

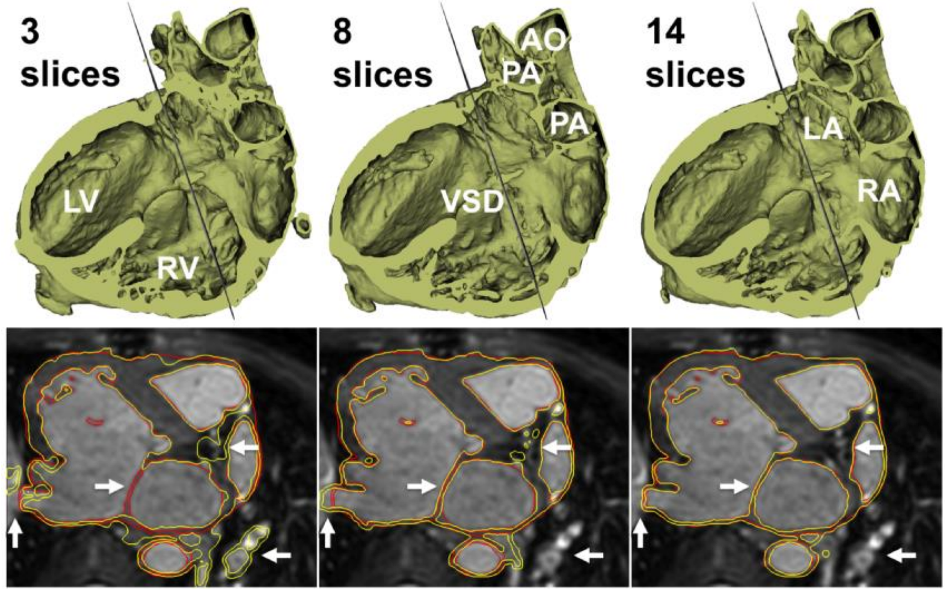
腦部中風區塊影像處理



Source : Adrian, Segmentation of Cerebrovascular Pathologies in Stroke Patient with Spatial and Shape Priors, 2014

醫療影像處理 – Case

心臟之心房，心室影像處理



2015, Danielle F Pace, “Interactive Whole-Heart Segmentation in Congenital Heart Disease”

COPD 病患之肺部影像處理

偵測器官輪廓、Tumor、Stroke、Lesion…

醫療影像處理議題

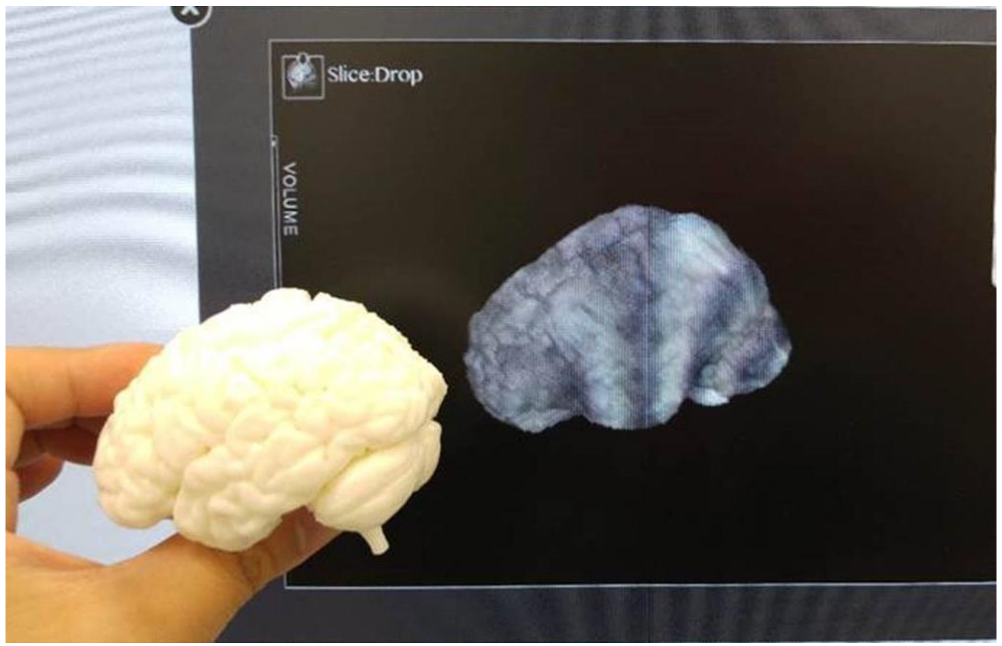
以電腦科學出發，醫療影像處理議題包括；

- 影像前處理 (前處理 or 提升影像品質)
    - 降噪
    - 差補
- 影像配準 (Image Registration) – 配準演算法
- 影像分割 (Image Segmentation) – 分割演算法
- 影像+臨床資料之統計模型 – 異質性資料分析
- fMRI

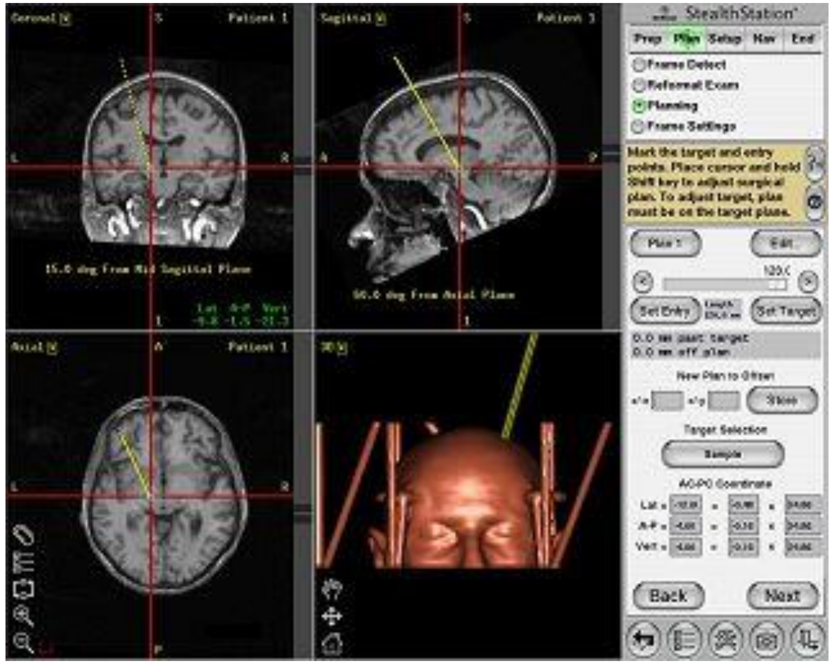
每個議題都充滿挑戰，因為我們事先都不知道身體裏面的實際狀況

醫療影像處理影用

- 3D Printing



- 手術導航



- Healthcare

Mortality Prediction Model

醫療影像處理技術-影像配準 (Registration)

- ✓ 影像配準 (Image Registration) 的目的，是將兩個影像對位
- ✓ 影像通常因為許多原因導致位移；例如掃描時病患身體移動，機器校正...原因
- ✓ 現行影像配準方法有；
    - Rigid 剛性配準：影像位移、旋轉，線性轉換
    - Affine 仿射轉換：影像位移、旋轉、放大/縮小
    - 投影：直線映射，但不保持平行性質
    - Non-Rigid : 即 Non-Linear Transformation, 非線性轉換
    - Information Theory; eg. Mutual Information…
- ✓ 配準模式可分為；
    - Monomodality 單模配準
    - Multimodality 多模配準

影像配準 基本原理

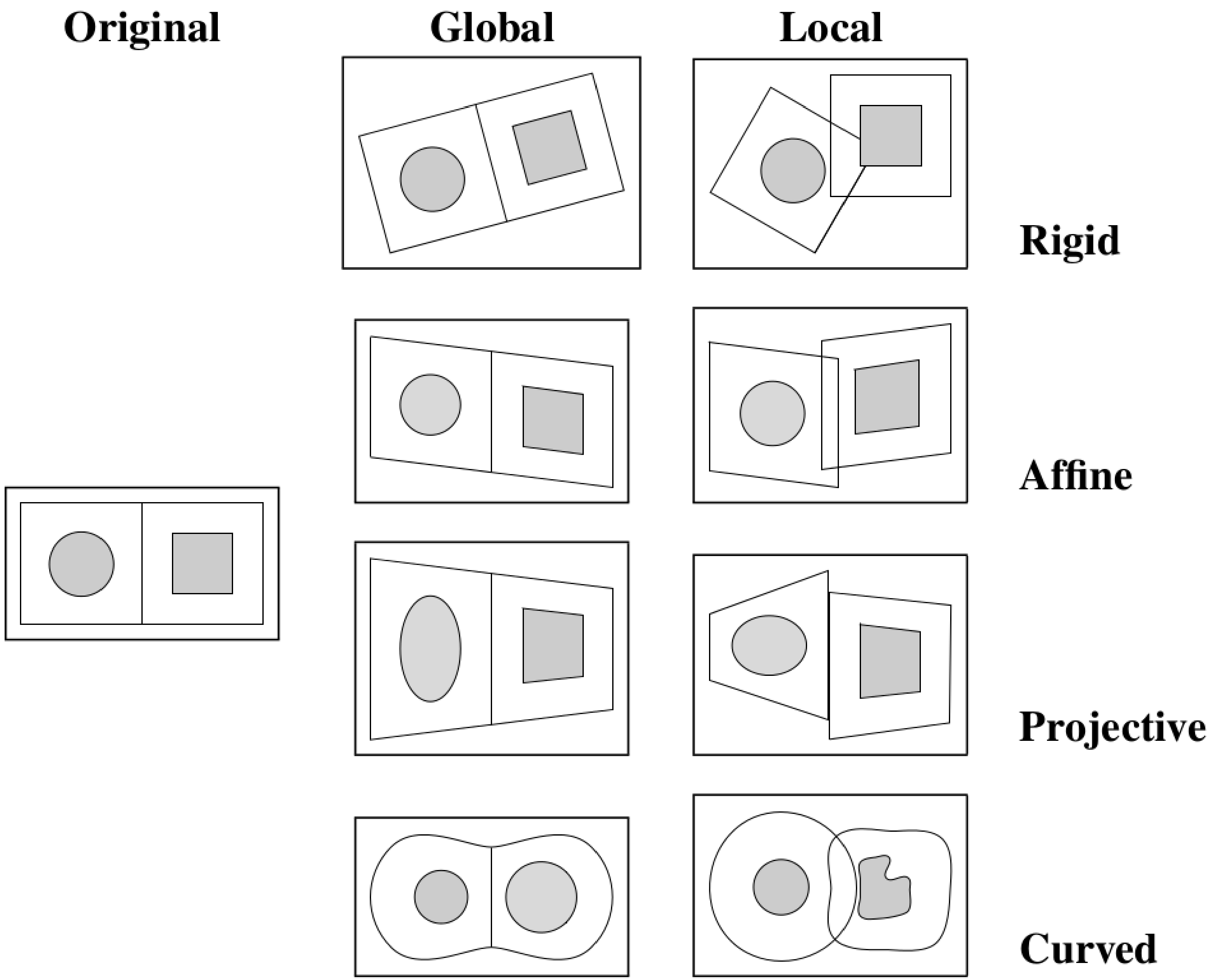


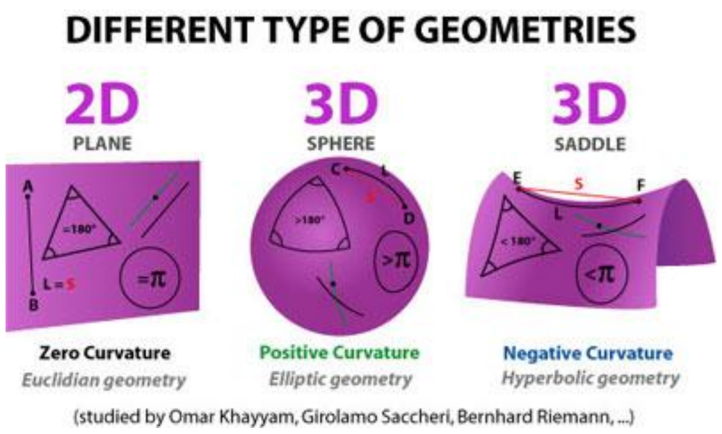
Figure 2: Examples of 2D transformations.

醫療影像處理技術-非線性配準

線性配準方法有他的限制，很自然的發展非線性配準方法 (nonlinear, non-rigid)

非線性配準方法大部份基於平行線原理，處理；

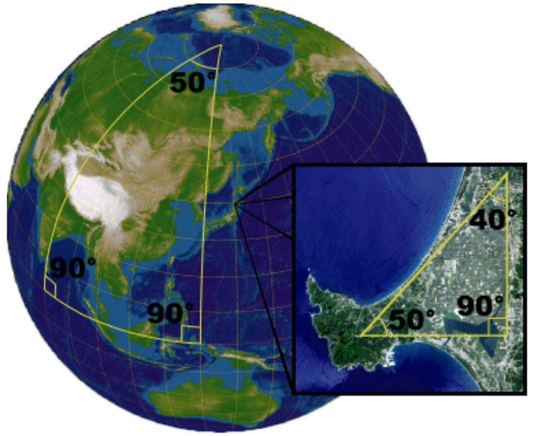
- 高維度資料處理
- 光滑平面 (流型, Manifold)
- 測地線最短距離 (Geodesic)



(1) 平行線會相交

(2) 三角形內角和不等於180

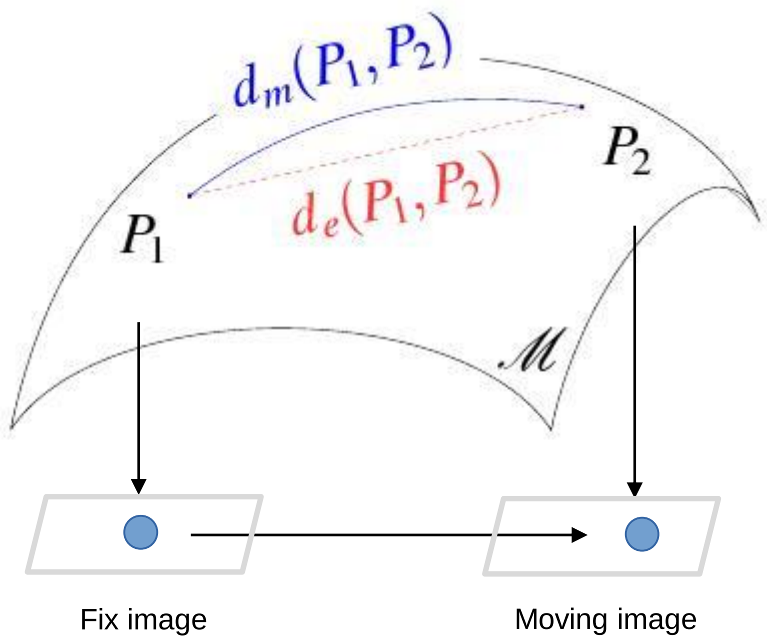
The easiest way to think of elliptic geometry is to consider a triangle drawn on a sphere. The interior angles sum to more than 180°, although, on a smaller scale, Euclidean geometry is a good approximation.



在球面上找最短距離

醫療影像處理技術-非線性配準

ANTs 的影像配準演算法 (SyN) 是強大的演算法,此演算法即基於找尋最短測地線為基礎的演算法。而測地線又由黎曼距離發展而來。



在平滑面上求距離(弧長)

非線性配準 – SyN 簡介

- 剛剛提到非線性配準，找最短距離很重要。
- SyN 的公式如下；

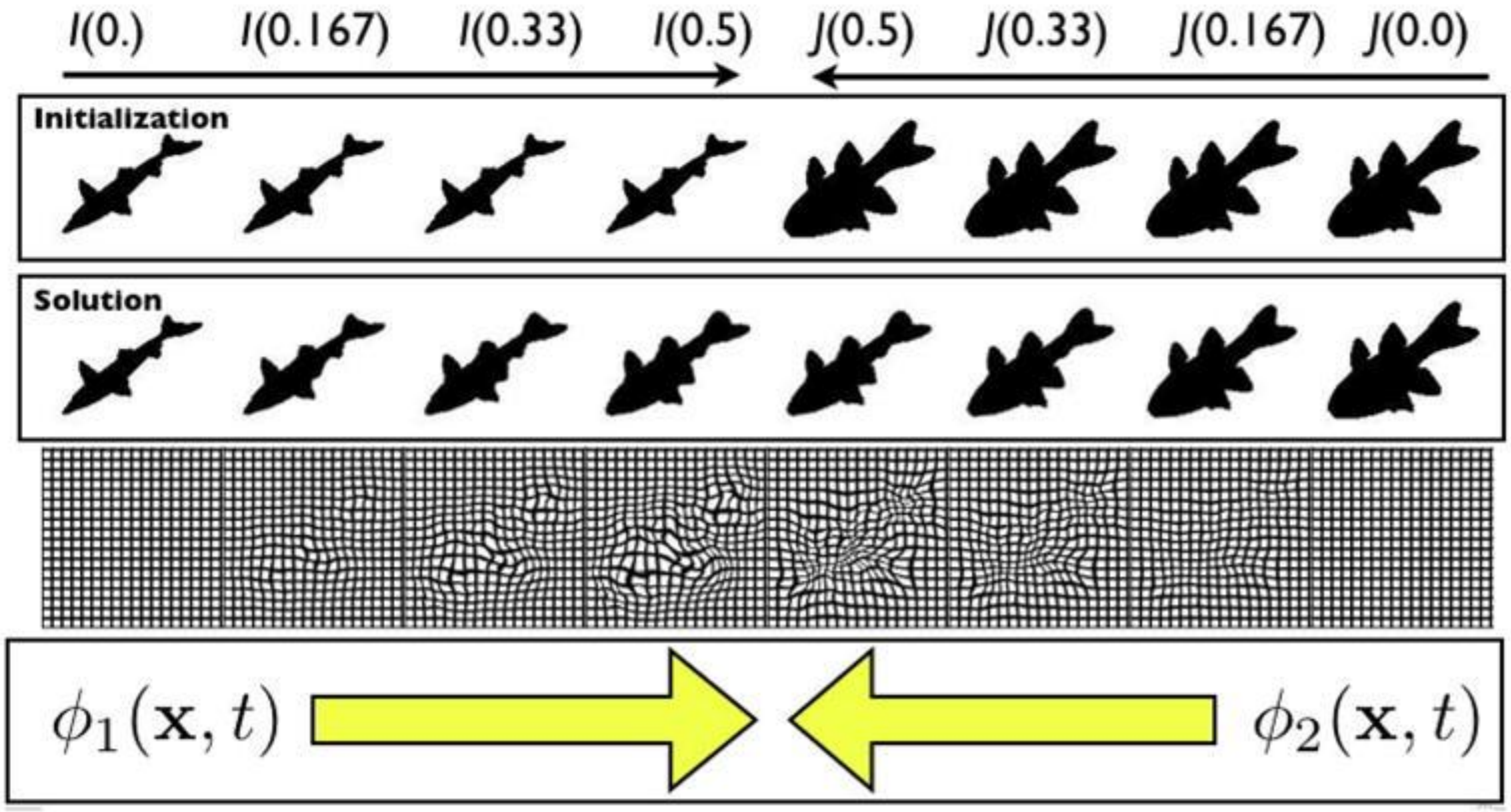
$$\boldsymbol{v}^* = \underset{\boldsymbol{v}}{argmin}\left\{\underline{\int_0^1 \|L\boldsymbol{v}\|^2 dt} + \lambda \underline{\int_\Omega \Pi_\sim(\mathcal{I}, \phi(x,1), \mathcal{J})d\Omega}\right\}$$

第一項：找測地線最短距離 **+** 第二項：找兩張圖之間相似度最高資訊

- CC
- Max Mutual Information

LDDMM (Large Deformation Diffeomorphic Metric Mapping) 是核心演算法

非線性配準 – SyN 簡介



I(0.)
I(0.167)
I(0.33)
I(0.5)
J(0.5)
J(0.33)
J(0.167)
J(0.0)
Initialization
Solution
$\phi_1(\mathbf{x}, t)$
$\phi_2(\mathbf{x}, t)$

醫療影像處理技術-配準方法彙整

Classification for medical registration methods

I. Dimensionality
- **a.** Spatial dimensions only:
  1. 2D/2D
  2. 2D/3D
  3. 3D/3D
- **b.** Time series (more than two images), with spatial dimensions:
  1. 2D/2D
  2. 2D/3D
  3. 3D/3D

II. Nature of registration basis
- **a.** Extrinsic
  1. Invasive
     - **A.** Stereotactic frame
     - **B.** Fiducials (screw markers)
  2. Non-invasive
     - **A.** Mould, frame, dental adapter, *etc.*
     - **B.** Fiducials (skin markers)
- **b.** Intrinsic
  1. Landmark based
     - **A.** Anatomical
     - **B.** Geometrical
  2. Segmentation based
     - **A.** Rigid models (points, curves, surfaces)
     - **B.** Deformable models (snakes, nets)
  3. Voxel property based
     - **A.** Reduction to scalars/vectors (moments, principal axes)
     - **B.** Using full image content
- **c.** Non-image based (calibrated coordinate systems)

III. Nature of transformation
- **a.** Rigid
- **b.** Affine
- **c.** Projective
- **d.** Curved

IV. Domain of transformation
- **a.** Local
- **b.** Global

V. Interaction
- **a.** Interactive
  1. Initialization supplied
  2. No initialization supplied
- **b.** Semi-automatic
  1. User initializing
  2. User steering/correcting
  3. Both
- **c.** Automatic

VI. Optimization procedure
- **a.** Parameters computed
- **b.** Parameters searched for

VII. Modalities involved
- **a.** Mono-modal
  1. Autoradiographic
  2. CT or CTA
  3. MR
  4. PET
  5. Portal
  6. SPECT
  7. US
  8. Video
  9. X-ray or DSA
- **b.** Multi-modal
  1. CT—MR
  2. CT—PET
  3. CT—SPECT
  4. DSA—MR
  5. PET—MR
  6. PET—US
  7. SPECT—MR
  8. SPECT—US
  9. TMS—MR
  10. US—CT
  11. US—MR
  12. X-ray—CT
  13. X-ray—MR
  14. X-ray—portal
  15. X-ray—US
  16. Video—CT
  17. Video—MR
- **c.** Modality to model
  1. CT
  2. MR
  3. SPECT
  4. X-ray
- **d.** Patient to modality
  1. CT
  2. MR
  3. PET
  4. Portal
  5. X-ray

VIII. Subject
- **a.** Intrasubject (1)
- **b.** Intersubject
- **c.** Atlas

IX. Object
- **a.** Head
  1. Brain or skull
  2. Eye
  3. Dental
- **b.** Thorax
  1. Entire
  2. Cardiac
  3. Breast
- **c.** Abdomen
  1. General
  2. Kidney
  3. Liver
- **d.** Pelvis and perineum
- **e.** Limbs (orthopedic)
  1. General
  2. Femur
  3. Humerus
  4. Hand
- **f.** Spine and vertebrae

- brief registration criterion description
- brief optimization procedure description
- validation (if any) used

Registration:
1. Problem statement (I,III,VII,VIII,IX)
2. Criterion (paradigm) (II,III,IV,V)
3. Optimization (V,VI)

Related:
- Validation
- Visualization/fusion

此表是彙整醫療影像配準方法，包含；

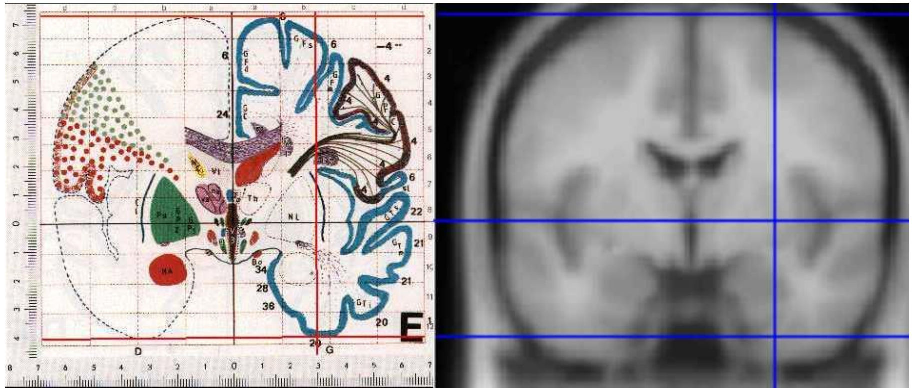
1. 影像的維度
2. 取得特徵方法
3. 轉換方法
4. 計算最佳化方法
5. 影像模式
6. 器官、部位

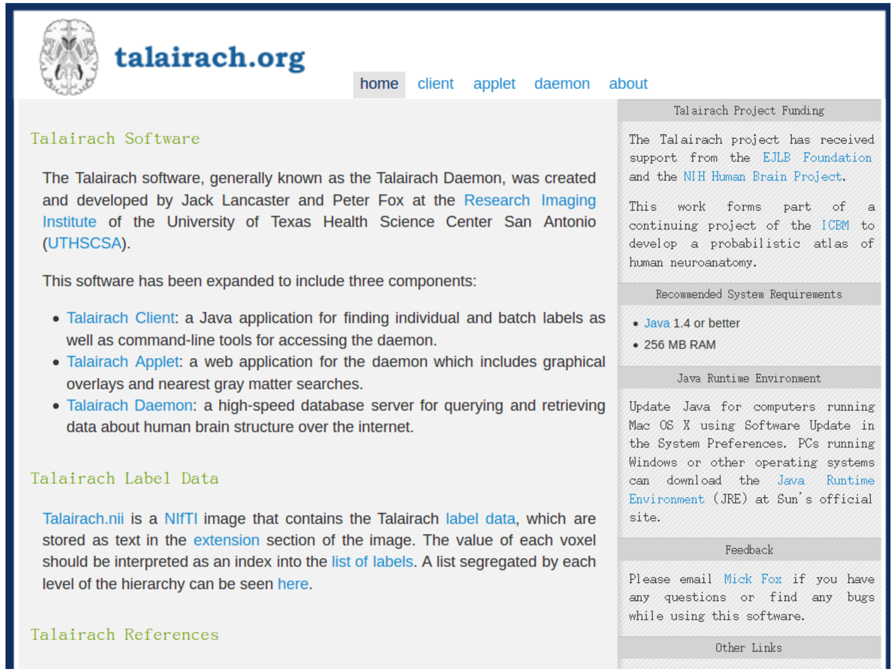
加上應用面，經交叉組合後，可發展出各式各樣的議題

Source : An Overview of Medical Image Registration Methods

醫療影像處理技術-Atlas

- 在無法剖開身體情況下，我們該用什麼當作 Ground-Truth?
- Talairach and Tournoux 兩位教授發展了一套腦部標準圖譜，(Atlas)。現在有幾個版本；
  - MNI305：55個掃描+250掃描結果配對到250圖譜
  - 現形標準版是 ICBM152
  - Colin27：MNI 實驗室的研究員 Colin 把自己的腦掃描27次發現配準狀況不錯，於是成為 Colin27





醫療影像處理技術-影像配準原理

在進入R程式碼之前，先介紹一些影像配準原理；

(1) Point Method : 在影像上作標記當作特徵點

(2) Curve Method : 分別對應兩條曲線，找曲率

(3) Correlation Method : 採用圖形間相似性最大原理配準

(4) Maximization Mutual Information : 也是一種兩個圖形相關性量測

(5) Atlas Method : 用標準圖來配準

以上為配準的基礎。配準做的好，才能提昇影像品質，進而後續的分析。

許多配準的方法為綜合上述原理開發演算法

醫療影像處理技術-影像分割(Segmentation)

✓醫療影像分割是另一個重要議題

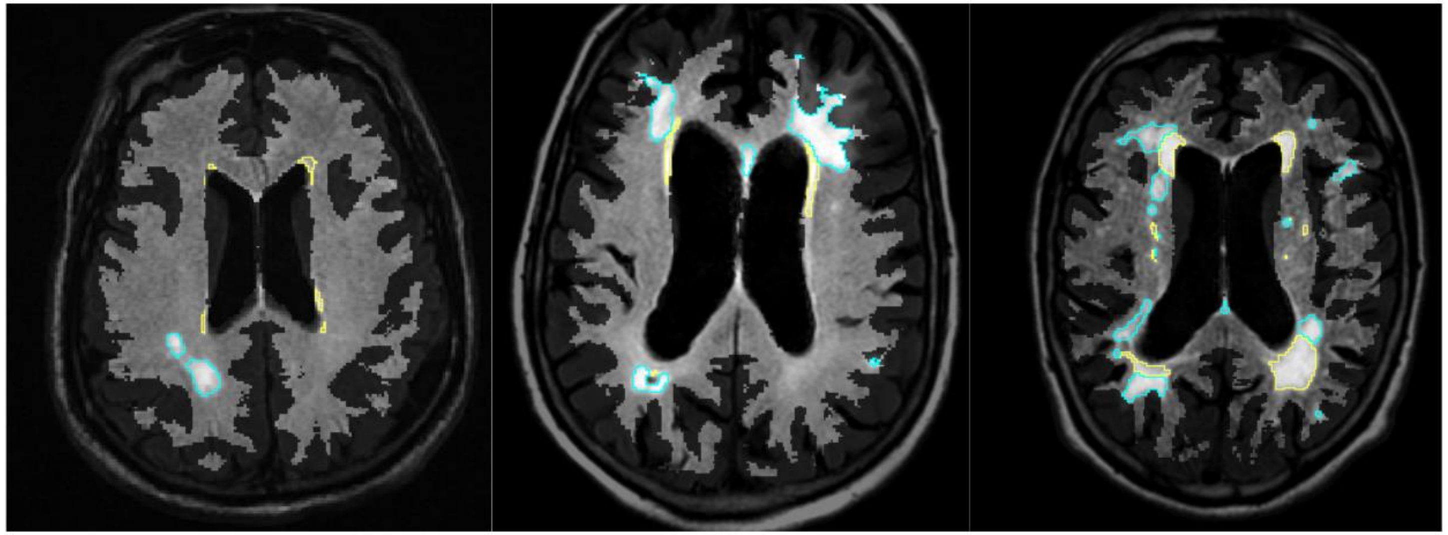
✓醫療影像分割不完全是 Edge Detection 的問題，因為組織可能有不同的形態；例如以 2014 MICCAI 分類中風這篇論文為例，當讀取一個 Voxel 後，判斷；

(1) 健康組織

(2) 中風組織

(3) 腦灰白質

✓演算法為病理師帶來的好處是；提供又快，又穩定的分析結果

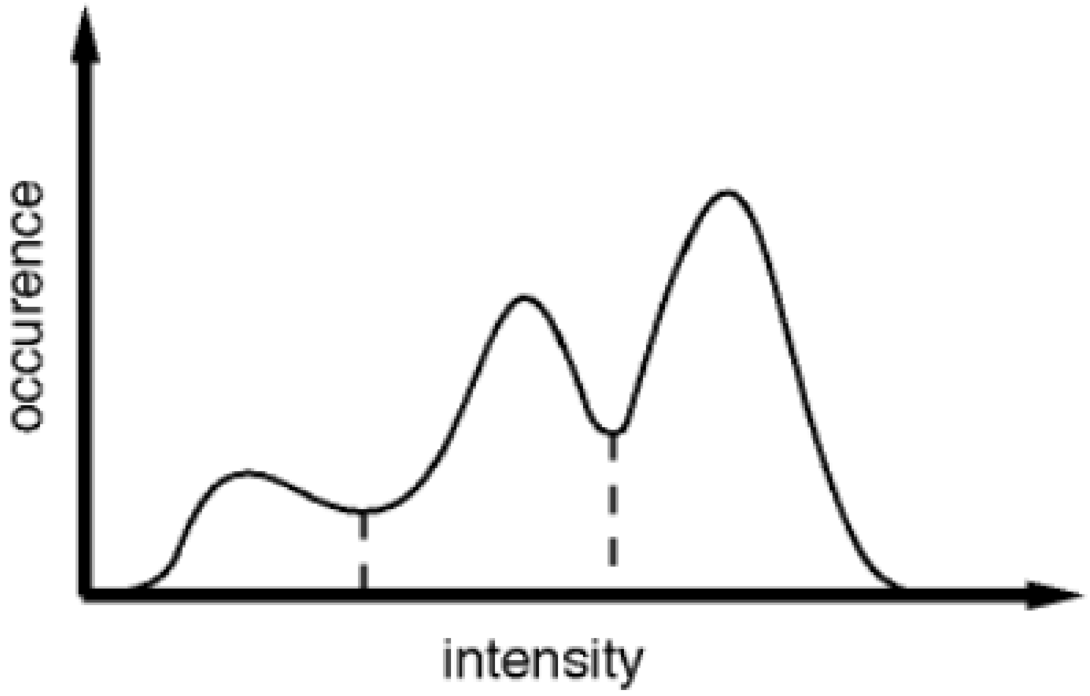


2014, MACCAI, Segmentation of Cerebrovascular Pathologies in Stroke Patients with Spatial and Shape Priors, Adrian Vasile Dalca

醫療影像處理技術-影像分割(Segmentation)

1). Thresholding 法

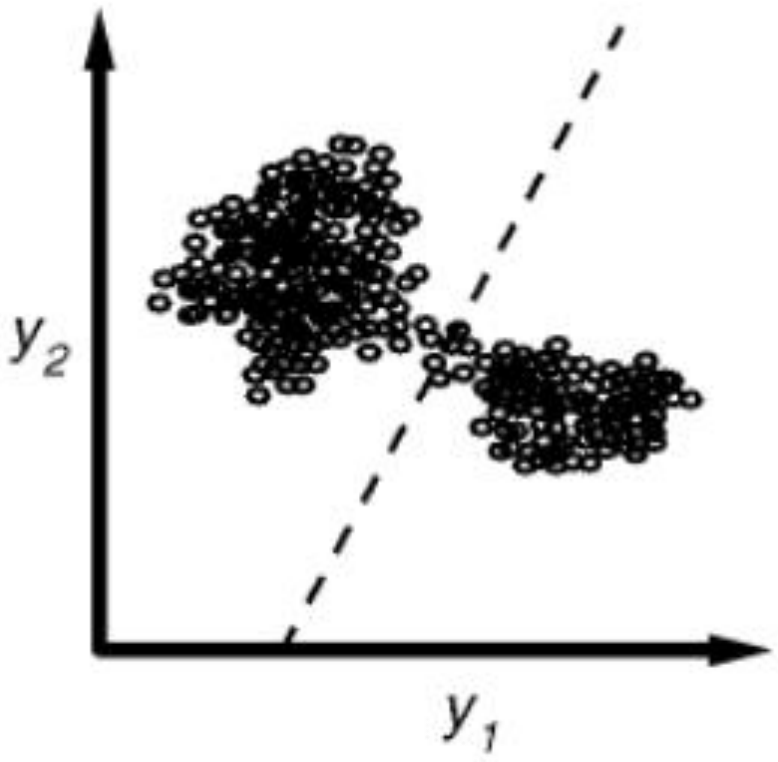
根據影像強度Intensity，給定門檻值下，做邊界分割



醫療影像處理技術-影像分割(Segmentation)

2). Classifier

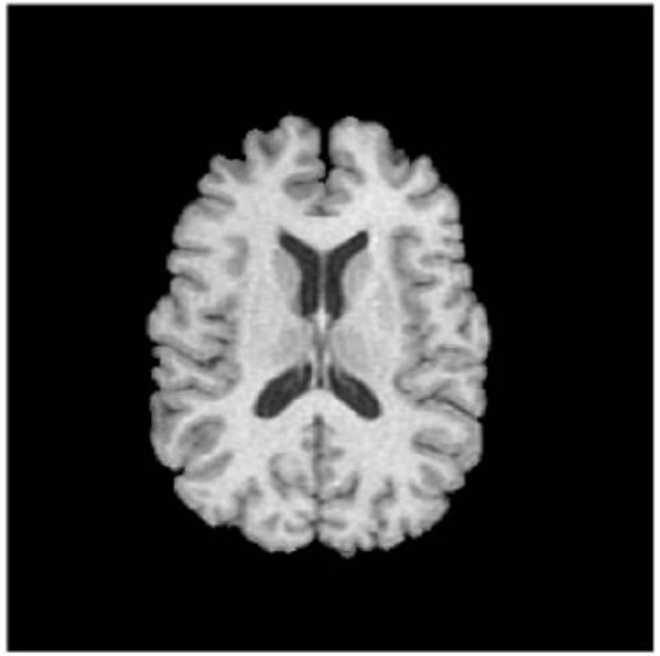
使用分類法(很多分類法)將影像分類

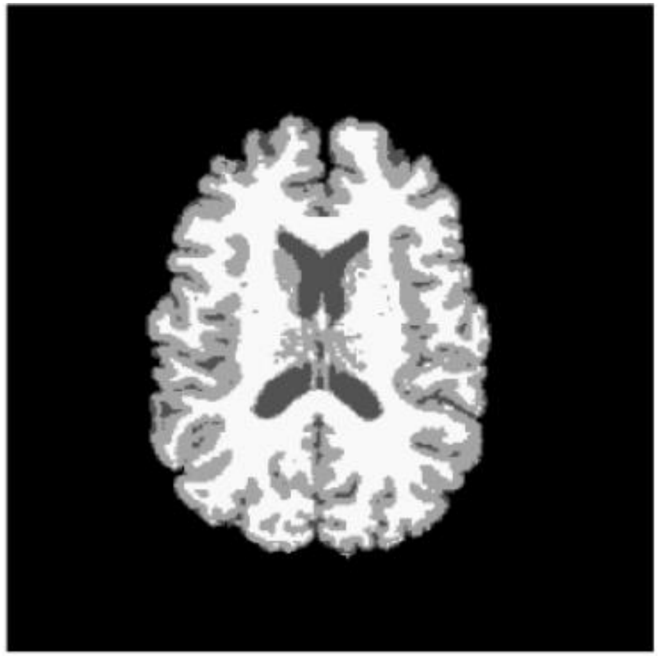


醫療影像處理技術-影像分割(Segmentation)

3). Clustering

使用分群法，將影像分類。下面是 K-mean 的分群結果範例。

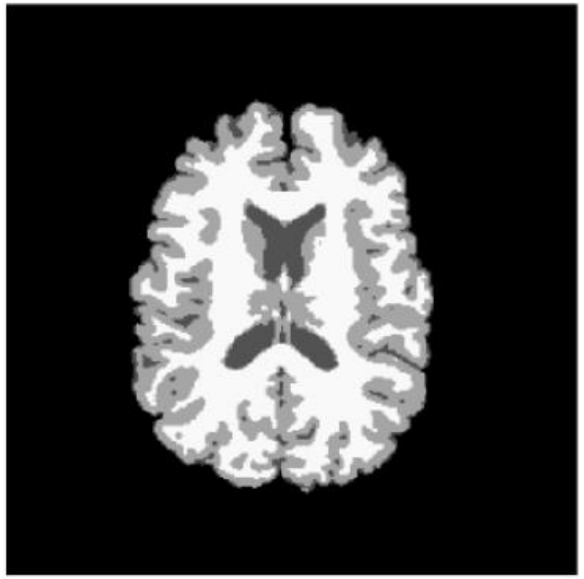




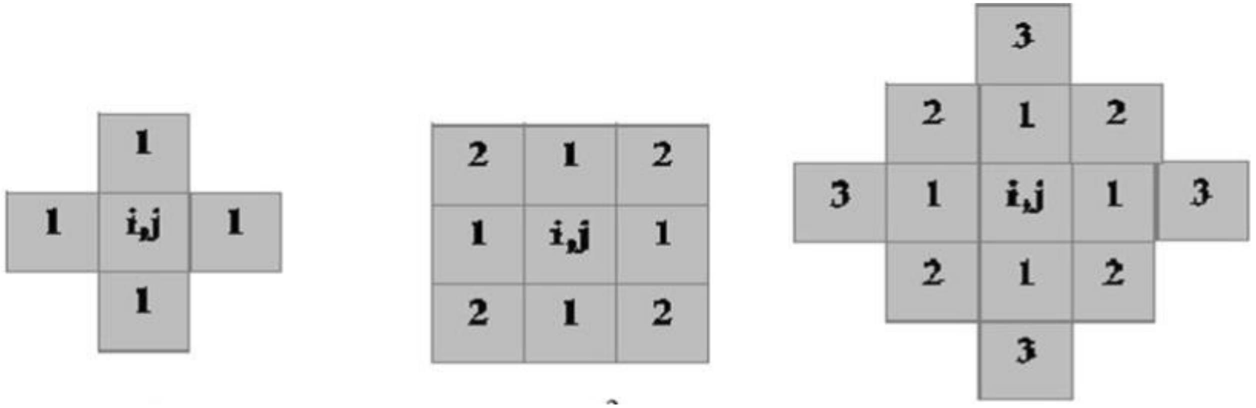
醫療影像處理技術-影像分割(Segmentation)

4). Markov Random Field

對於目標Pixel (voxel)，根據四周的點判斷



(c)



中間的 Pixel (voxel) 會參考四周的影像來決定設個 pixel 的分類結果

醫療影像處理技術-影像分割(Segmentation)

最近最熱門就是使用 Deep Learning 方法了。MICCIA有70%的論文在討論 Segmentation，其中 Deep Learning 又占了大部分。這一篇是 PathAI 這家公司提出分析乳癌切片影像分類。

AI-ENABLED DIGITAL PATHOLOGY PathAI

SOLUTION. Tumor detection through Deep Learning using Convolutional Neural Network.

CHALLENGE

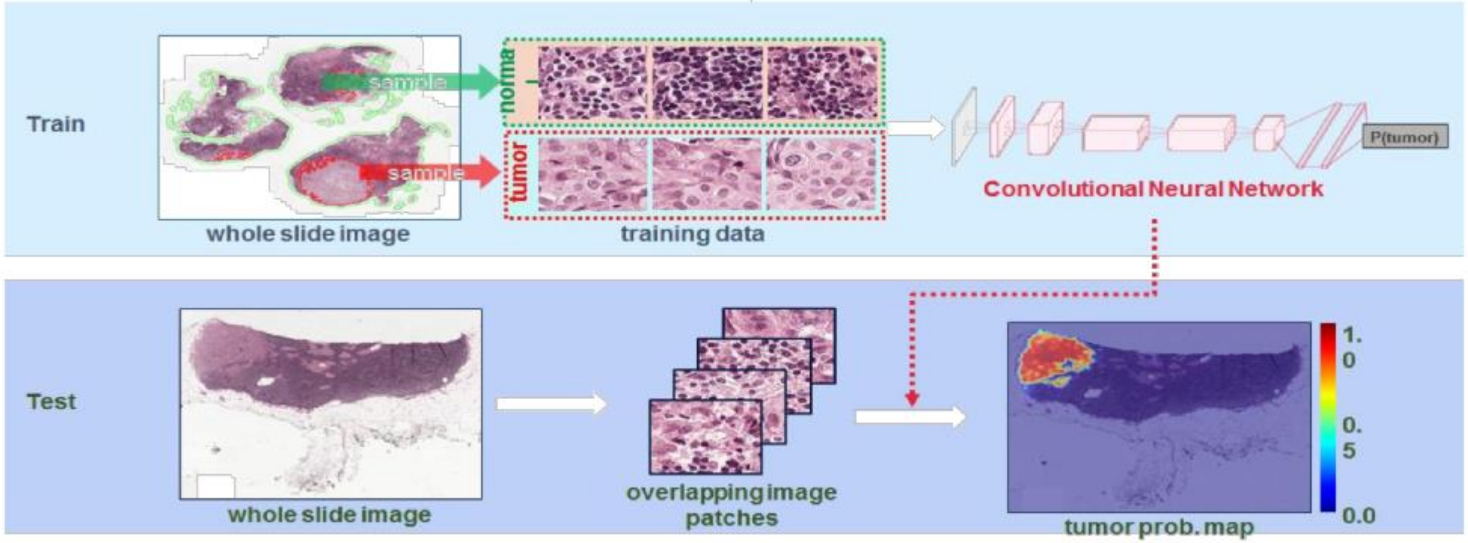
Though automated mitosis detection approach human-level performance, this is achieved in more controlled conditions when mitosis detection is performed in pre-selected regions of relevant tumor tissue.

To be more practical, mitosis detection must be applied to whole-slide images (WSIs).

IMPACT

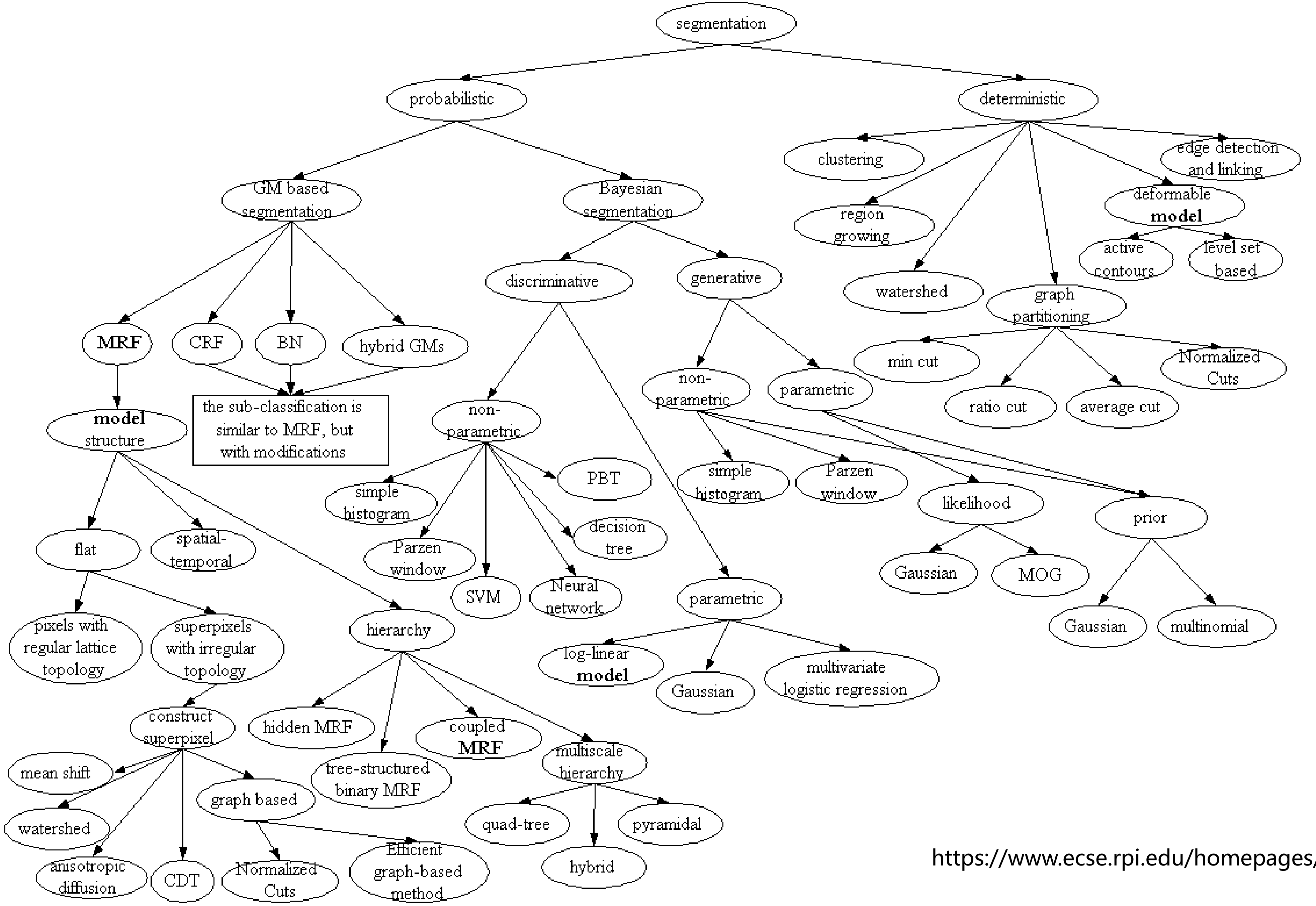
99.5% accuracy achieved by combining pathologists' analysis, with automated computational diagnostic. Automated diagnostic method proved accurate approximately 92% of the time, nearly matched the success rate (96%) of human pathologist.

The system enables higher accuracy diagnosis and early detection.



Source: Breast Cancer News, MICCAI TUPAC 16

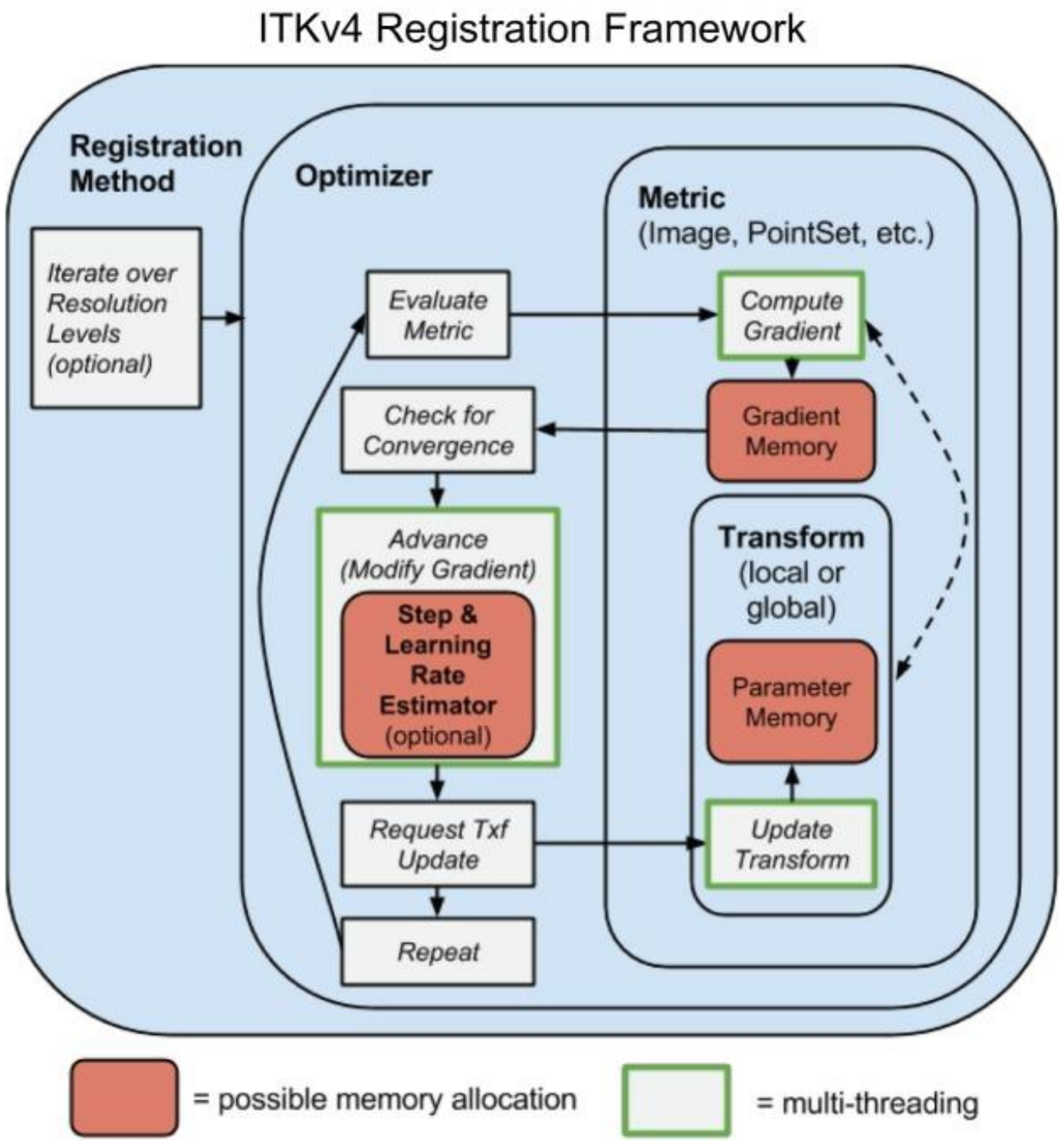
有高手將 Segmentation 做成一張地圖



https://www.ecse.rpi.edu/homepages/cvrl/lei/segmentation_ontology.htm

ITK (Insight ToolKit) 簡介

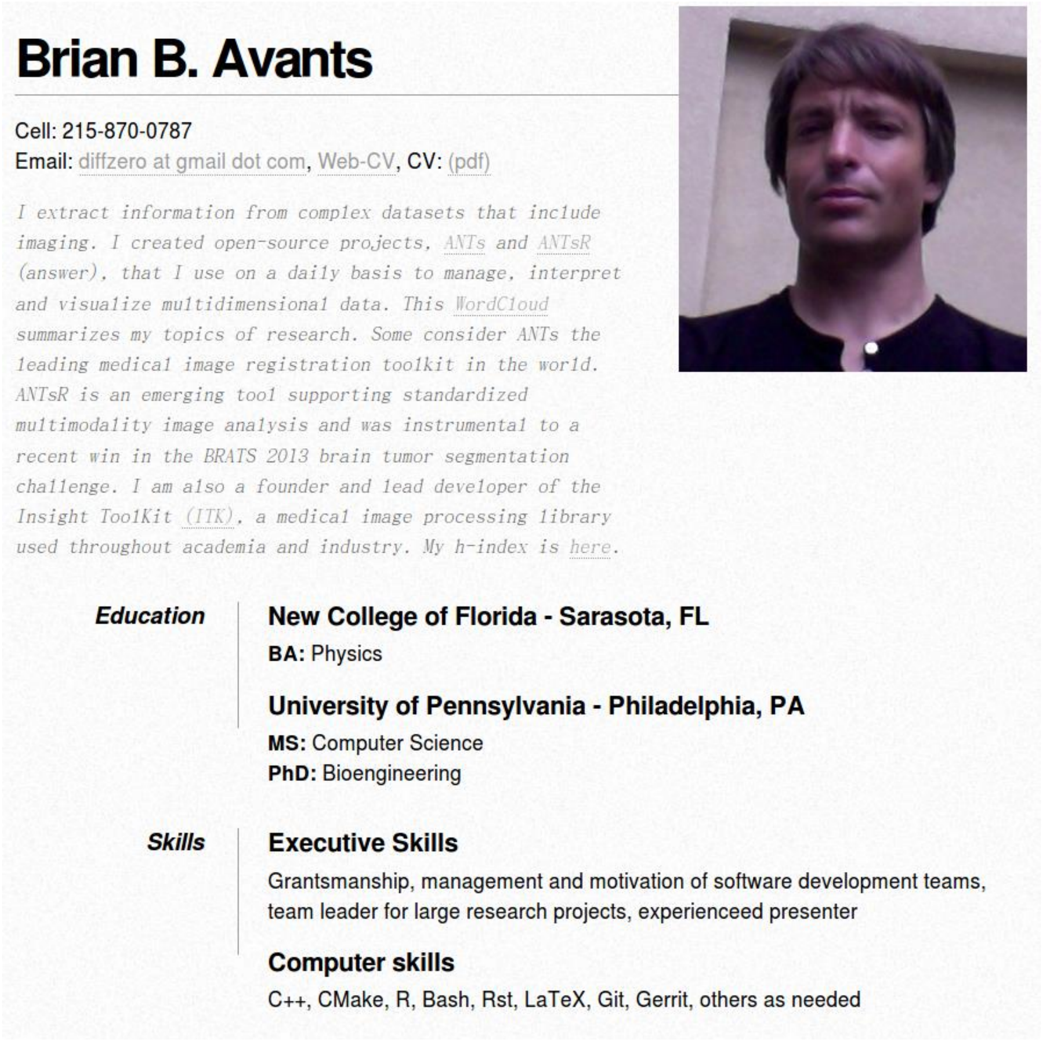
- 1999 : US National Library Of Medicine of NIH (National Institutes of Health) 得到6年的計劃開發醫療影像 配準 and 分割工具，即稱為 ITK。合作的單位有 GE. MathSoft, UNC(北卡大學), UT(田納西大學), Utah(猶他大學), UPenn(賓州大學)
- 2002 發表開始第1版工具ITK 提供了影像處理底層架構，ANTs即基於 ITK 的架構下發展演算法



ANTsR 的簡介

Provide a general purpose library of multivariate image registration, segmentation & statistical analysis tools。

UPenn 的Brian Avants 教授是 ANTs 和 ANTsR 的創始人



Brian B. Avants

Cell: 215-870-0787
Email: diffzero at gmail dot com, Web-CV, CV: (pdf)

I extract information from complex datasets that include imaging. I created open-source projects, ANTs and ANTsR (answer), that I use on a daily basis to manage, interpret and visualize multidimensional data. This WordCloud summarizes my topics of research. Some consider ANTs the leading medical image registration toolkit in the world. ANTsR is an emerging tool supporting standardized multimodality image analysis and was instrumental to a recent win in the BRATS 2013 brain tumor segmentation challenge. I am also a founder and lead developer of the Insight ToolKit (ITK), a medical image processing library used throughout academia and industry. My h-index is here.

Education

New College of Florida - Sarasota, FL
BA: Physics

University of Pennsylvania - Philadelphia, PA
MS: Computer Science
PhD: Bioengineering

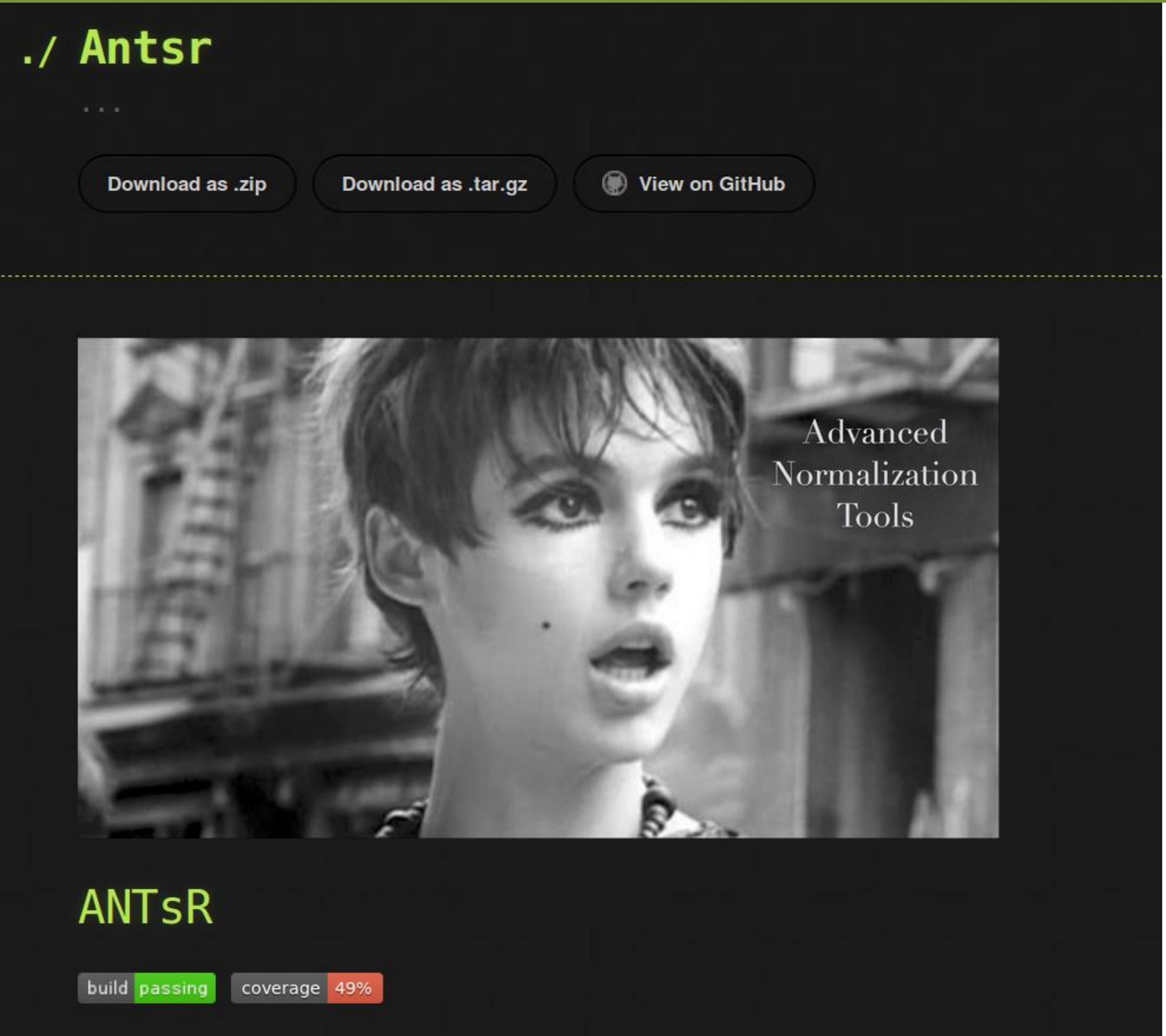
Skills

Executive Skills
Grantsmanship, management and motivation of software development teams, team leader for large research projects, experienceed presenter

Computer skills
C++, CMake, R, Bash, Rst, LaTeX, Git, Gerrit, others as needed

ITK + ANTs + R = ANTsR

ANTsR 的官方網頁



ANTsR 是這兩年發展的工具，官方網站有 MANUAL、Tutorial、GitHub 有一些 Source Code 但可以還是有許多可發展的空間。

官方網站超連結

ANTsR 的 Package 文件

Package ‘ANTsR’

January 19, 2016

Type Package

Title ANTs in R

Version 0.3.2

Author Brian B. Avants, Benjamin M. Kandel, Jeff T. Duda, Philip A. Cook, Nicholas J. Tustison, Shrinidhi KL

Maintainer Brian B. Avants <stnava@gmail.com>

Description ANTsR interfaces state of the art image processing with R statistical methods. The project grew out of the need, at University of Pennsylvania, to develop large-scale analytics pipelines that track provenance from scanner to scientific study. ANTsR wraps an ANTs and ITK C++ core via Rcpp to access these frameworks from within R and support reproducible analyses.

License GPL (>=2)

LazyLoad yes

Depends methods

Imports Rcpp, tools, magrittr

Suggests abind, BGLR, caret, cluster, d3Network, DMwR, e1071, extremevalues, fastICA, fpc, glasso, glmnet, grid, igraph, knitr, magic, MASS, mFilter, misc3d, moments, pixmap, png, psych, randomForest, rgl, robust, robustbase, RRedsvd, signal, sna, testthat, visreg, wmtsa

LinkingTo Rcpp, ITKR

CRAN 上有 ANTsR 的文件，但安裝需要花一些時間。官方建議安裝在 Linux 或 MacOS 上

今天介紹來 ANTsRHandout

Advanced Normalization Tools Quick Reference

Brian B. Avants

2016-08-08

等一下會透過這份文件，介紹一些 ANTsR 的功能

Introduction

Advanced Normalization Tools[1] is software for biomedical image analysis with a focus on registration, segmentation, geometric quantification and statistics. Statistical methods are available in *ANTsR* [2] which tightly integrates *ANTs* with the *R* statistical computing language. This document briefly highlights *ANTs* features.

[1] http://stnava.github.io/ANTs/

[2] http://stnava.github.io/ANTsR/

點我 Github 連結

Provenance and Testing

Much core functionality in *ANTs* lives in ITK, a project to which we contribute regularly. This core is tested on many platforms via `ctest` and the results are on the ITK dashboard[3]. *ANTs* is also tested with every commit via codeship [4] and Travis [5]. Many (not all) *ANTs* programs support `programName --version`. Our github commit hashes give the best way to track code versions by identifying core and dependency versions. See the *ANTs* website for current testing results and **installation** instructions.

[3] https://open.cdash.org/index.php?project=Insight

[4] https://codeship.com

[5] https://travis-ci.org/stnava/ANTs

In conjunction with other analysis systems

ANTs and ITK work synergistically within a well-defined I/O and world coordinate system. Using FSL, SPM or other pre-processing in conjunction with ITK and *ANTs* must be done with extreme care. The physical spaces (or interpretation of image headers) may not be the same in different systems. Such inconsistencies may lead to severe misinterpretation of results.

WARNING!

今天介紹來 ANTsRHandout

```r
library(ANTsR)

# Step 1 : Read sample brain image
# fi = fix image
# mi = movinf image
fi <- antsImageRead(getANTsRData("r16"))
mi <- antsImageRead(getANTsRData("r64"))
invisible(plot(fi))
invisible(plot(mi))

# Use "Rigid" to linear register image
# antsApplyTransforms
mytxr <- antsRegistration(fixed = fi, moving = mi,typeofTransform = c("Rigid"))
mywarpedimager <- antsApplyTransforms(fixed = fi,
                                      moving = mi,
                                      transformlist = mytxr$fwdtransforms)

# Use "SyN" to non-linear image
start_time<-Sys.time()
mytx <- antsRegistration(fixed = fi, moving = mi,
                         typeofTransform = c("SyN"))
end_time<-Sys.time()
totaltime=end_time-start_time
totaltime
#
mywarpedimage <- antsApplyTransforms(fixed = fi,
                                     moving = mi,
                                     transformlist = mytx$fwdtransforms)
# Canny, Edge Detector
invisible(plot(fi, mi %>% iMath("Canny", 1, 5,12)))
invisible(plot(fi, mywarpedimager %>% iMath("Canny",1, 5, 12)))
invisible(plot(fi, mywarpedimage %>% iMath("Canny",1, 5, 12)))
```

先跑一些基本的影像處理

(1) Rigid 轉換

(2) SyN 轉換

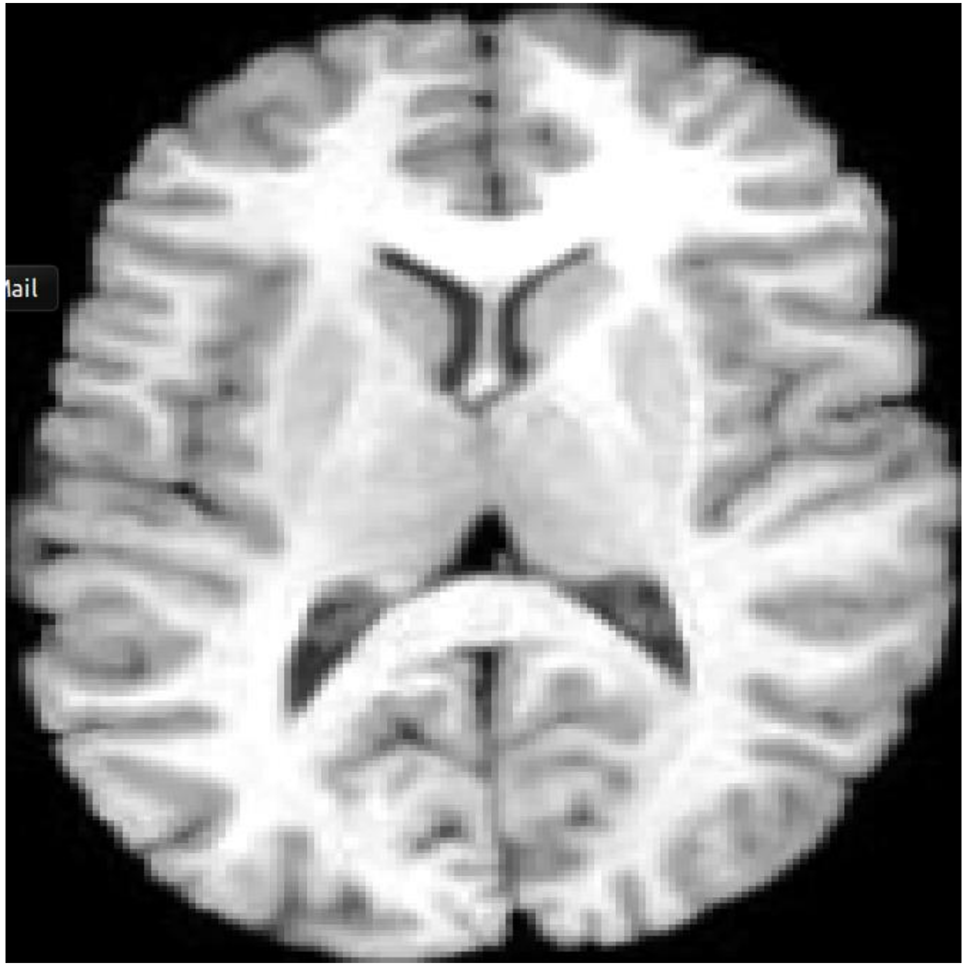
看看兩個方法轉換後的結果

原始影像

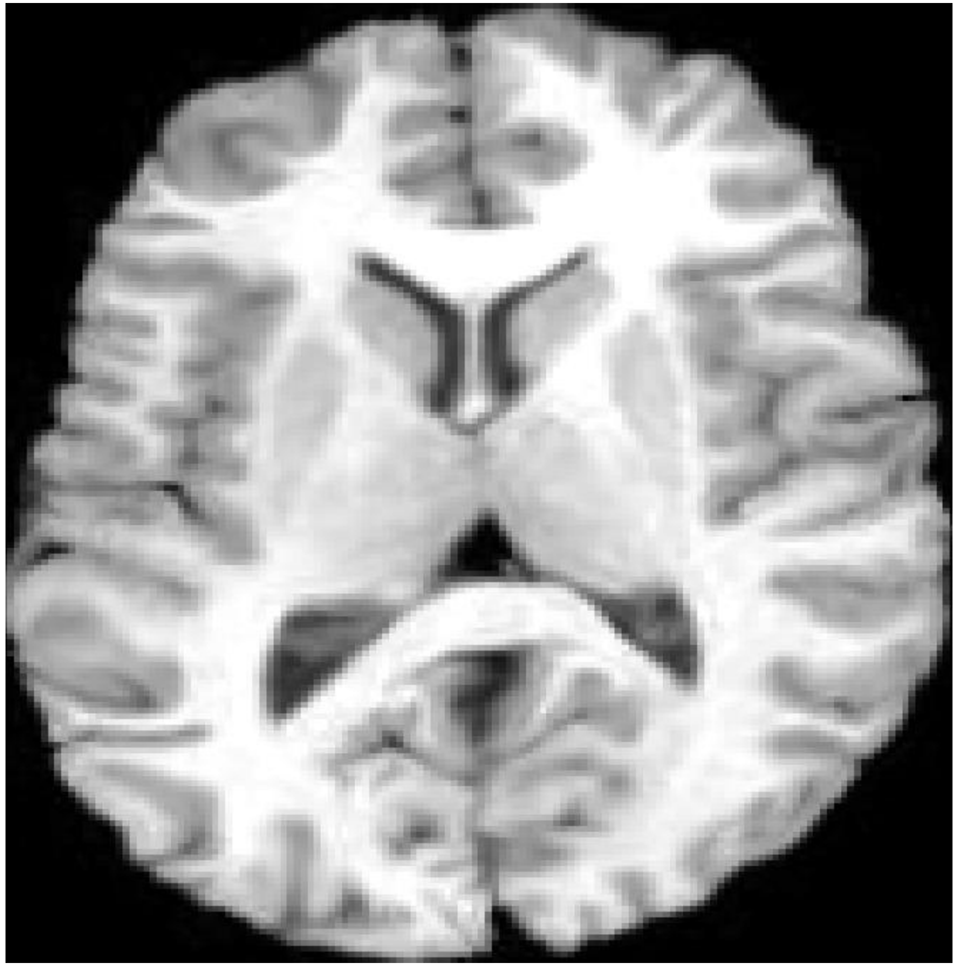
這張是參考腦部影像，稱為 Fixed Image
簡稱 ***fi***

這張是待配準的腦部影像，稱為 Moving Image
簡稱 ***mi***

計畫一下配準所花費時間



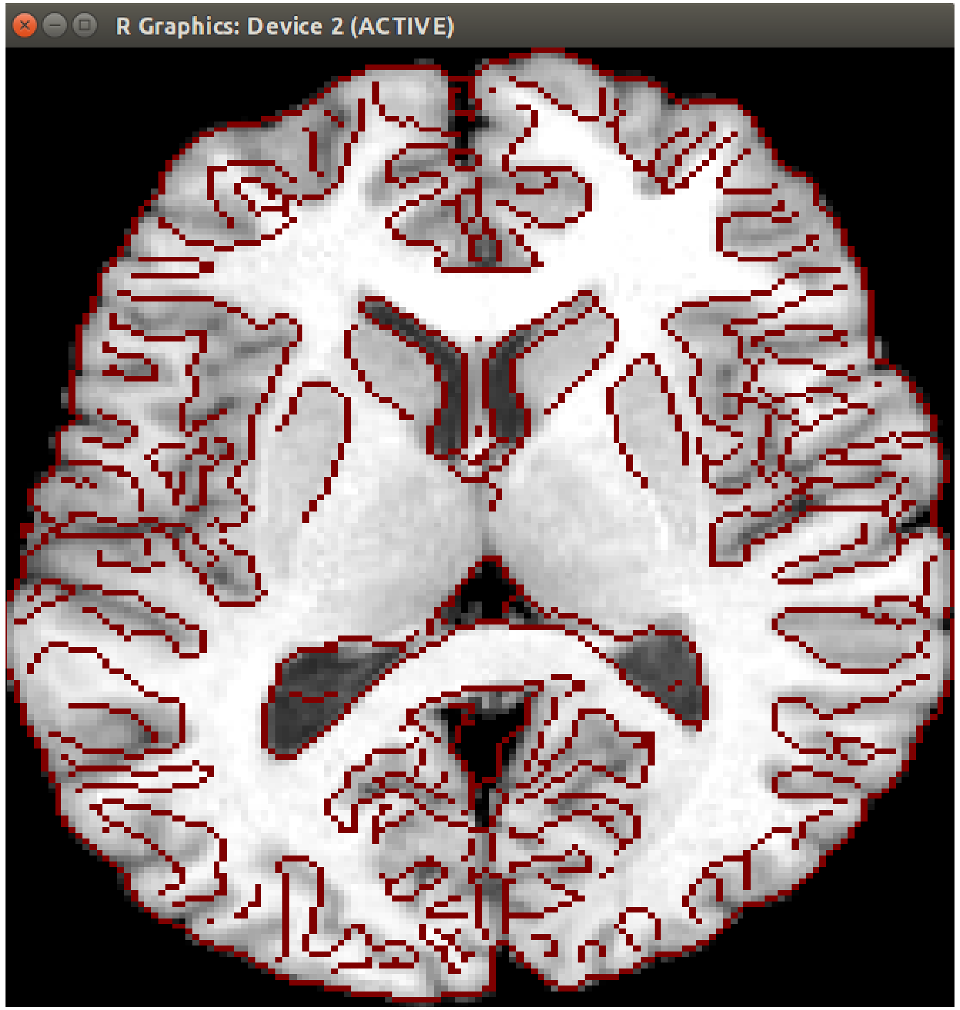
Rigid 配準演算法結果，約花費0.3秒



SyN 配準演算法結果，約花費2秒

Side by Side 比較

左邊是 Rigid 配準的結果



右邊是 SyN 配準的結果

大家覺得哪邊的配準效果比較好??

影像強度均勻校正演算法- N4

Corruptted Image

Fixed Image, 修復後的影像

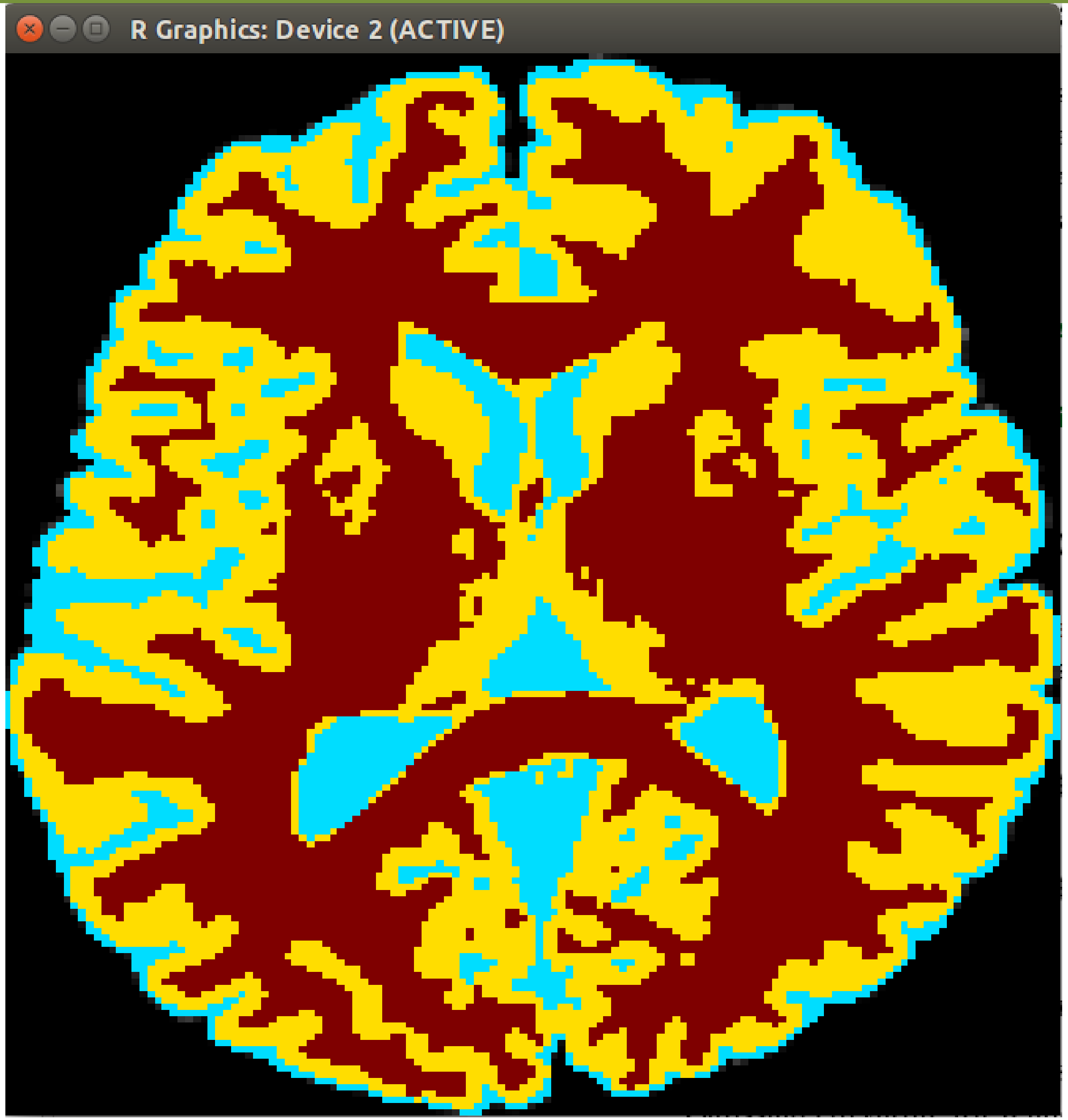
K-mean + Atropos 影像分割演算法

```
# Atropos
img <- antsImageRead(getANTsRData("r16"))
mask <- getMask(img)
segs1 <- kmeansSegmentation(img, 3, mask)
# Use probabilities from k-means seg as priors
feats <- list(img, iMath(img, "Laplacian"), iMath(img,"Grad"))

st3<-Sys.time()
segs2 <- atropos(d = 2, a = feats, m = "[0.2,1x1]",
                 c = "[2,0]", i = segs1$probabilityimages,
                 x = mask)
end3<-Sys.time()
total3=end3-st3
total3

invisible(plot(fi, segs1$segmentation))
invisible(plot(fi, segs2$segmentation))
```

1) K-mean, 分3群

2) Atropos，EM演算法一種

K-mean + Atropos 影像分割演算法



K-mean =3 的結果

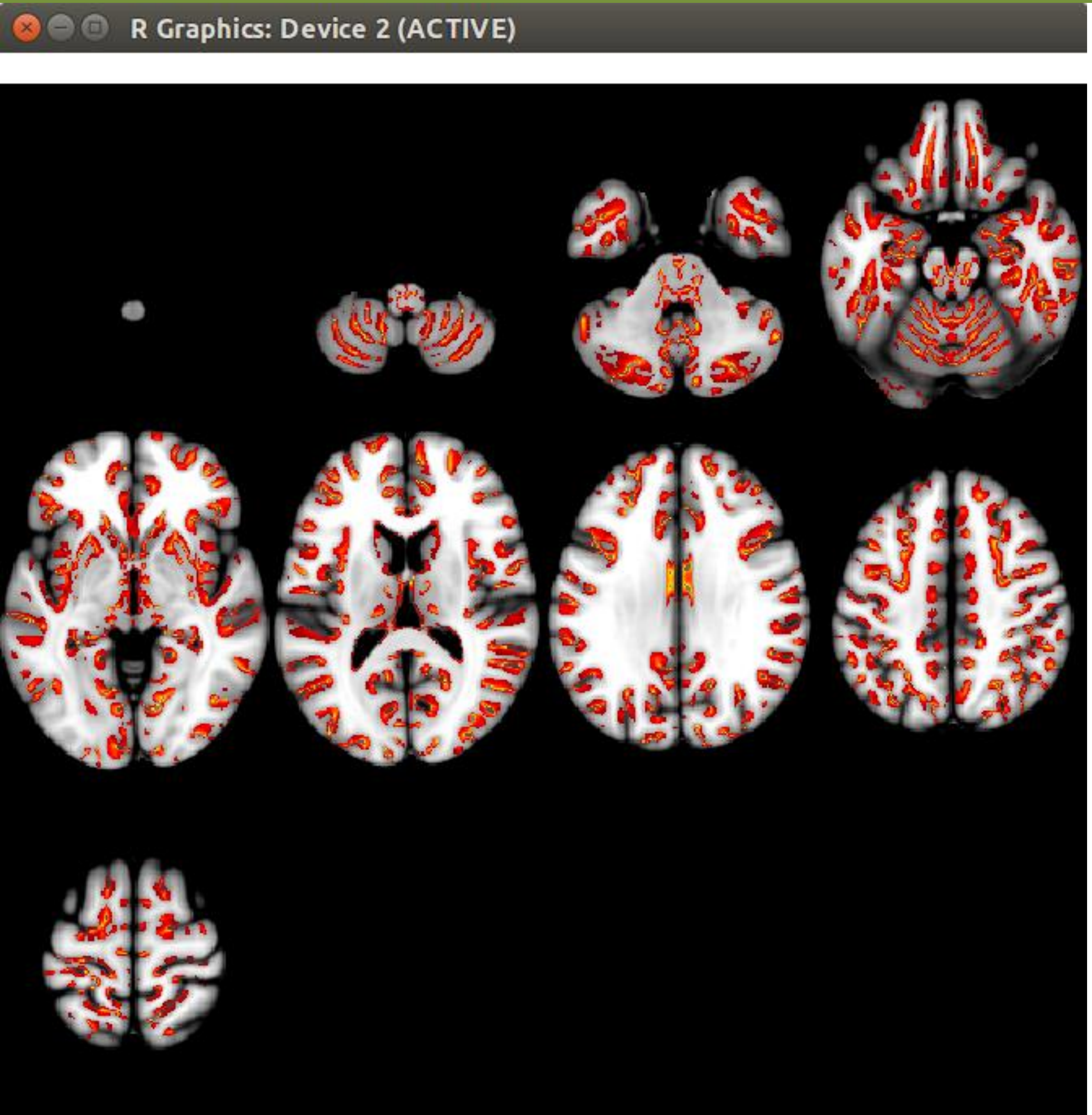
Atropos (EM) 演算法結果

SurfaceCurvature

```r
# Map surface curvature
fi <- antsImageRead(getANTsRData("mni"))

start4<-Sys.time()
fiseg = kmeansSegmentation(fi, 3)
fik <- weingartenImageCurvature(fi)
# invisible(plot(fik, axis = 3))
fisulc = antsImageClone(fik) * 0
selector = (fiseg$segmentation == 2 & fik < 0)
fisulc[selector] = fik[selector]
end4<-Sys.time()
totaltime4=end4-start4
totaltime4
invisible(plot(fi, fisulc, axis = 3))
```

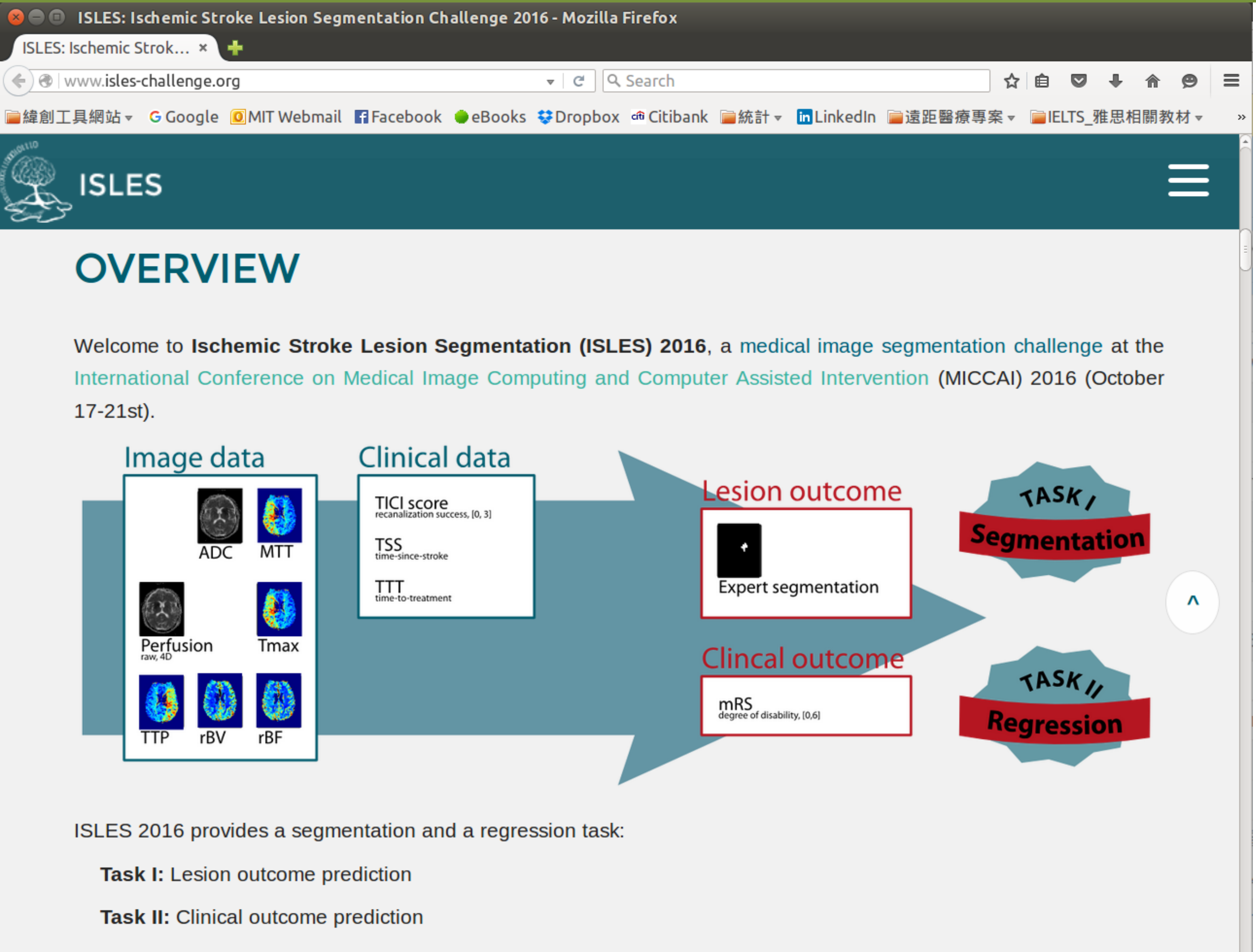
我們來產生更漂亮的腦部分割結果

SurfaceCurvature



這短短的演算法花了3分鐘，主要時間花在影像生成

每年的 ISLES 比賽



這是 “缺血性中風腦部影像” 挑戰賽。每年跟 MACCAI 研討會一起舉辦

主要分兩個任務，

(1) 影像分割 (拚速度 and 精確度)

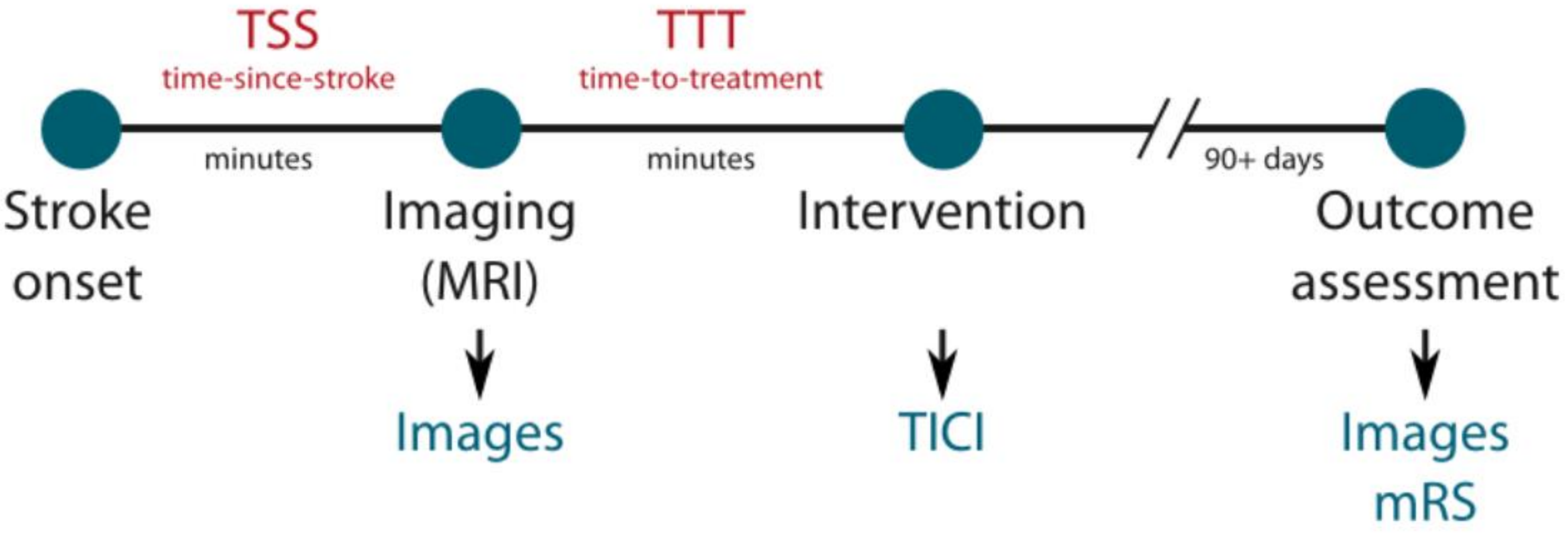
(2) 結合相關指標，例如 mRS (調整後雷式指標)，做病患的預測

[網站連結]

每年的 ISLES 比賽 - 動機

MOTIVATION

The typical stroke treatment procedure involves the acquisition of brain images at some time-since-stroke (TSS). Depending on the these and other factors a treatment decision is made and an intervention takes place after a time-to-treatment (TTT). The success of this intervention is assessed via the standardized TICI score. After the effects stabilized, the final clinical outcome is determined with the mRM and the final lesion outcome by brain imaging.



醫療影像的商業模式

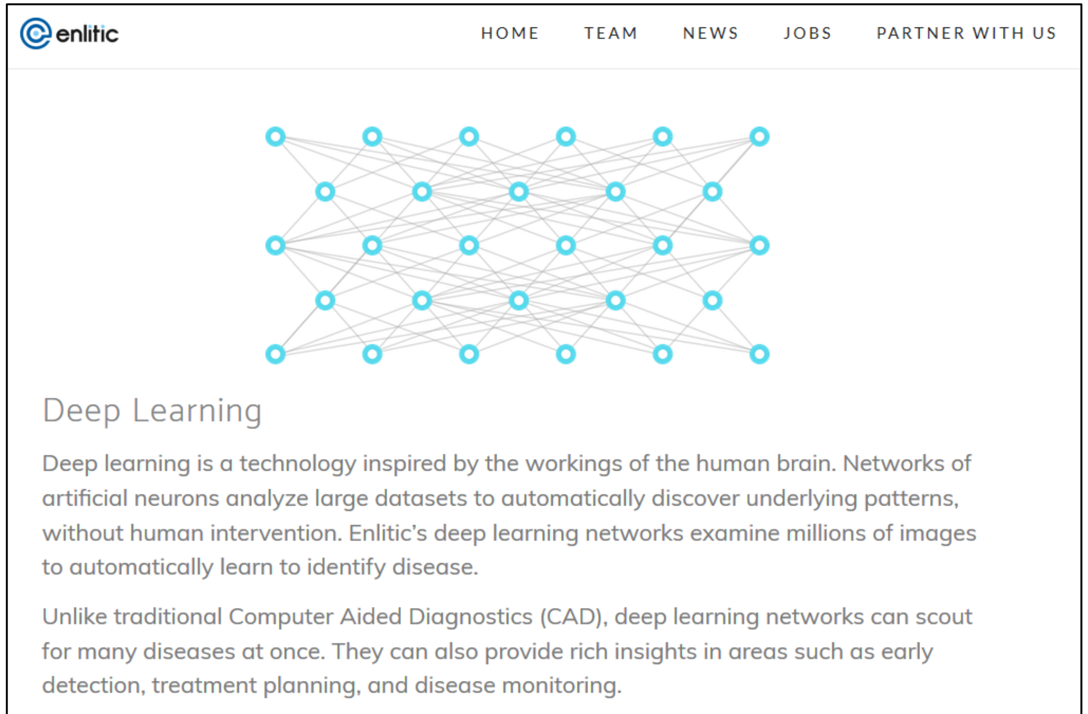
Medical Image 潛在商業模式；

(1) 演算法賣給 Philips, GE, 西門子

(2) 新創外包看片(判片)公司，提供快速、穩定分析的服務. eg, Entilic

(3) AR, 3D Printing, Healthcare Prediction…

Entilic 網站



歡迎大家一起腦力激盪…

謝謝你的聆聽

Q&A