Design of a system to achieve diagnosis of brain lesions of suspected infectious origin from a database and a radiologic software.


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Leukocytes, leukemia

White blood cells, leukocytes, are used by the body to fight infections and other foreign substances. Leukemia is a type of blood cancer that begins in the bone marrow (the soft tissue in the center of the bones, where blood cells are produced).

Leukemia Cells:
the body produces large numbers of abnormal blood cells. In most types of leukemia, the abnormal cells are white blood cells. The leukemia cells usually:
• look different from normal blood cells, and
• they do not function properly.
Treatment(s), side effects, complications

There are typically three treatment stages for the average-risk patient with ALL:

- **Induction therapy** to achieve a first remission (the absence of active cancer)
- **Consolidation** to prevent relapse after remission has been achieved
- **Maintenance treatment** to prevent relapse after remission (given for several years)

Leukemia can also spread to the brain and spinal cord, most patients need chemotherapy (injected into the layers around them). It is the primary treatment for each stage

Some patients also need radiation to the brain

This is called **central nervous system prophylaxis** and is given during all treatment phases to prevent the cancer from spreading to the brain and spinal cord

A bone marrow transplant may be recommended after treatment

Infection from partial or total suppression of the immune system is a common and serious side effect. Patients should make all efforts to prevent infection and minimize exposure to bacteria and viruses. The patient at high risk for infection may need very potent antibiotics and antifungal medications

Invasive fungal infections (IFIs) remain an important cause of morbidity and mortality in patients with acute or chronic leukemia.

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**Figure 1**

Pie charts showing the evolving epidemiology of invasive fungal infections by their prevalence in autopsies of patients with leukemia at M. D. Anderson Cancer Center, Houston, Texas.
Introduction

Purpose and benefits

At present, diagnosis of brain infections is very complex due to location and hard interpretation of radiologic images. As brain infections in immunosuppressed oncohaematologic patients undergoing chemotherapy or transplant of haemopoietic stem cells have the worst prognosis, diagnostic images must be made easier to understand and more homogeneous, so as to apply targeted treatments as quick as possible.

This project aims at creating an international database including an extensive collection of radiologic images of brain lesions and the relevant clinical, laboratory and microbiological data. Based on this, an "intelligent" software will be developed. Multi-dimensional analysis techniques, variational methods, classification procedures, as well as neural networks and Bayesian forecasting models will be used to detect, highlight and differentiate the minimal and yet peculiar differences in the "radiologic footprint" related to the local alterations of brain tissue produced by each individual pathogen. That will become an objective diagnostic tool that is not influenced by the operator’s interpretation.

We planned the following steps:
1. Design and implementation of the database hosting biological data and radiological images
2. Develop diagnostic and radiological followup protocols, currently not available for this kind of complications and these target patients
3. Develop a software to perform elastic image registration to achieve better image comparison against a template and combine clinical and radiological data to obtain the probability of presence of a specific pathological agent

Many data required =>
MULTICENTRE PROJECT
Architecture, data workflow

1. web site (apache, php, joomla)
2. database interface (php)

web server www.brainsupporters.eu

1. database server (mysql)
2. image analysis software (ITK, imageJ, ...)
3. statistical analysis (octave, R... object of next future talk[sl])
4. data fusion and integration algorithm (...object of next future talk[s])

data analysis, hosted by CNR-ISMAR brainsupporters.ve.ismar.cnr.it
The collaboration site and the database are actually hosted on a **mysql** server, running on a virtual server on CNR-ISMAR (Ve)
The image database will be stored on **raid5 nas (10TB)**

Main tables are:
- **at_patients**: patient data: like birth date, sex…
- **ht_patients_primary**: first patient examinations data
- **ht_patients_followup**: biological data from every followup

Radiological images (CT, NMR) will be
- uploaded as a single compressed file to be decompressed and
- stored in DICOM format

Images are connected to the patient and its clinical data
Every information in the database is related to an **uploader**
Every uploader must belong to a **centre**
Every uploader has access to
- his data and (eventually)
  - anonymized data from the other uploaders

The **collaboration weight** is estimated and used to give access to data from other uploaders

At this stage, every centre may contribute in defining/refining the protocol
- Clinical data and images are automatically processed every time new data are uploaded to the database and
- results (templates and statistic results from biological data) are accessible to every centre
Image processing measures and statistical analysis

- **Image filtering (denoise)**
  we are looking for small lesions
  salt and pepper noise should be removed while preserving edges

- **Feature space analysis**
  at the beginning of the process lesions are difficult to find
  (because of low contrast) thus
  we wish to enhance image readability and
  obtain a first ROI selection from automatic segmentation

- **Coregistration and template generation** is required
  we have many images to compare with each other and against a template
  we aim to follow patient evolution in time and
  we aim to find «anomalies»

- **Measures** (to achieve data fusion/data integration)
  «distance» $\text{image}_n$-template/$\text{image}_i$-image$_j$ (for MultiDimensional Scaling)
  geometrical, morphological, statistical evaluation[s] …
Single image denoise
MINMAX2 algorithm

Motivation

• Borders are small if compared with a region
• A region comparable with a pixel may be regarded as noise
• Average filters reduce noise (reducing signal variability) but destroy borders

Theoretical Basis

• Gradient of an image is an edge detector
• Max gradient occurs when orthogonal to an edge
• Small changes in gradient direction preserve edges

We change signal variability while preserving edges by minimal changes in gradient direction

\[
S(p^*, r) := \left\{ p(x_1...x_n) \mid r + x^*_{i=1...n} \leq x_{i=1...n} \leq +r + x^*_{i=1...n} \right\}
\]

\[
\begin{cases}
\min_{I(\bar{p} \in S(\bar{p}^*, r))} > \min_2 \left( I(\bar{p} \in S(\bar{p}^*, r)) \right) \\
\max_{I(\bar{p} \in S(\bar{p}^*, r))} > \max_2 \left( I(\bar{p} \in S(\bar{p}^*, r)) \right)
\end{cases}
\]

\[
\min_2, \max_2 \text{ II order min and max}
\]
MINMAX2 to remove salt and pepper noise

Original (ideal) image

Corrupted image

Filtered image

not affected by noise

what we have are images affected by noise

MINMAX2 image r=10

our goal is to obtain the ideal image from the corrupted one
MINMAX2 in action

Original image I (with noise)  Filtered image J  Difference (noise..?)

J=MINMAX2(I,r=1)  I-J
**EDI: Entropy Distribution Image**

**Motivation**
- To compare multimodality images we need to alter signal values by a transformation or
- generate a feature space image from the 2 images
- according that value in the new images refer to the same physical observable

**Theoretical Basis**
- Shannon theory
- Entropy
- Information

\[
H(X) = - \sum_{i=1}^{N} p_i \cdot \log(p_i)
\]

\[
\Delta I = - \left[ H(X_1) - H(X_0) \right]
\]

\[
H(X_0) \quad \text{entropy BEFORE the transmission}
\]

\[
H(X_1) \quad \text{entropy AFTER the transmission}
\]

is a measure of the information required to transmit a signal (an \( n \)-bit symbol among \( k \)) on a channel, from a source to a target. It is also a measure of the entropy reduction due to the loss in uncertainty about the state of the target system.

It is possible to generate an image assigning to any pixel/voxel a value equal to the mean entropy of the symbol (bit sequence) in source image. Such an image is an **Entropy (spatial) Distribution Image**
EDI to find unnoticeable details

Measures: physics  Analysis: map generation

our goal is to put in evidence **unnoticeable details**

Original (ideal) image

MAP (image) in Feature Space

Original image combined with EDI map from feature space

noise is unnoticeable at this resolution

flash scattered light
We may obtain information from EDI map

Measures: physics  Analysis: map generation

Original image  MAP (image) in Feature Space

NMR image  EDI
We may obtain information from EDI map

Measures: physics
Analysis: map generation

Original image
MAP (image) in Feature Space

NMR image
EDI
We may obtain information from EDI map

Measures: physics  Analysis: map generation

original image

CT image

MAP (image) in Feature Space

EDI
**LEF: Local Entropy Filter**

**Motivation and Theoretical Basis**

**Motivation**
To answer the questions:
- which is the entropy distribution of the image if ROI of a given size are considered/investigated?
- is there an optimal rescale for this kind of image?

**Theoretical Basis**
- The mean entropy on a squared ROI of a given size is computed starting from point \((x,y)\) or \((x,y,z)\)
- an image is generated assigning this value to \((x,y)\)

\[
H_W : W \subseteq I \rightarrow s
\]

\[
s(\tilde{q}) = -\frac{1}{k} \sum_{\tilde{p} \in W(\tilde{q}, r)} f_{\tilde{p}} \log_2 (f_{\tilde{p}})
\]

\[
k = (2^r + 1)^n
\]

\[
W(\tilde{q}, r) = \{\tilde{q}_1 - r \leq \tilde{p}_1 \leq \tilde{q}_1 + r, \ldots, \tilde{q}_n - r \leq \tilde{p}_n \leq \tilde{q}_n + r\}
\]

\[
f_{\tilde{p}} = \frac{N_{\tilde{p}}}{N}
\]

\[
N_{\tilde{p}}(\tilde{p}) = I(\tilde{p})
\]
LEF map to find details at a given scale

Measures: statistics  Analysis: map generation

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**our goal is to put in evidence**

*unnoticeable details at a given scale*

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*Original* (ideal) image  MAP (image) in Feature Space  Original image combined with the map from feature space

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**wall texture**

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LEF image \(r=2 \ L=5\)  HSV2RGB
LEF map to find details at a given scale

Measures: statistics

Analysis: map generation

Original image

MAP (image) in Feature Space

MAP (image) in Feature Space

NMR image

LEF image $r=1$ $L=3$
detail order of magnitude: $27 \text{ mm}^3$

LEF image $r=2$ $L=5$
detail order of magnitude: $125 \text{ mm}^3$
Image model and coregistration problem

Given an ideal image (the template) \( I(x, y) \)

a real image may be modelled by the following equation

\[
H(x, y) = I(x, y) + D(x, y) + M(x, y) + \eta(0, \sigma)
\]

Given a transform \( T \) acting on images

\[
T_{\{p_1, p_2 \cdots p_n\}}(I) = J
\]

We wish to find the best values for \( T \) parameters satisfying the following equation:

\[
\lim_{(p_1, p_2 \cdots p_n) \to (p^*_1, p^*_2 \cdots p^*_n)} \| M(p_1, p_2 \cdots p_n)(x, y) \| \to 0
\]
Image coregistration and deformation field

our goal is to compare images

Subject A

Subject B

A+B

A-B

Rigid registration

Warp based registration

Requirement: invertibility of the deformation field to preserve geometry

Instead of comparing images we may compare deformation fields against a template
Coregistration example

NMR image  CT image  EDI images combined in feature space  scalar field obtained from the deformation field
Summarizing
This project aims at creating an international database including an extensive collection of radiologic images of brain lesions and the relevant clinical, laboratory and microbiological data, and a software, to highlight and differentiate the minimal alteration in the radiologic footprint related to the local alterations of brain tissue produced by each individual pathogen that will become an objective diagnostic tool.
Clinical parameters will be taken into account in defining a measure to estimate the probability that the difference between an image and a template be due to a specific pathological agent.

This is in ambitious project but we started our work and the project has been appreciated. We'll do our best

* A little job well done is the first step toward a bigger one.*
References