Imagine 2029: Our data, our health, our care – 20th anniversary of EHTEL

EHTEL 2019 Symposium

14:30 – 16:00 [S4]

Artificial Intelligence as a Trustful Enabler for Better Health and Better Care

Session Chair: Stephan Schug, EHTEL

Aula 1
First Floor

AI in practice: Enabling a Smart Phone for Predicting, Detecting and Staging Disorders
Jan Stener Jørgensen, CIMT, Odense University Hospital, Denmark

AI Applied to Screening for Diabetic Retinopathy
Aïda Valls, Rovira i Virgili University, Tarragona, Catalonia, Spain

AI for Diagnosis and Treatment of Infectious Diseases
Carolina Garcia, Hospital Clinic of Barcelona, Spain

AI for Diagnosis and Treatment in Dermatology
Marc Combalia, Hospital Clinic of Barcelona, Spain

Deep Lung: Deep Learning in Imaging for Better Detection and Assessment of Lung Cancer
Vicent Ribas Ripol, Eurecat Technology Center, Barcelona, Spain

Q&A and Conclusions by the Session Chair

#EHTEL_Symposium #EHTEL_BCN @ehtel_eHealth
Monitoring and detection of very early signs of preeclampsia (PE) by automatic image processing of pregnant women’s faces captured by daylight cameras

Jan Stener Jørgensen
Prof. MD PhD
CIMT - Odense University Hospital
Denmark
In the EHTEL program announced as:

AI in practice: Enabling a Smart Phone for Predicting, Detecting and Staging Disorders
Preeclampsia definition

- Pregnancy-related
- Syndrome
  
  (5 [3-15] % of all pregnancies)

- after 20 weeks gestation
Preeclampsia definition

Manifestations

• varying degrees of **hypertension**

• **proteinuria**
  - and/or to a variable extent:

• **other organ involvement**
  - liver,
  - kidney,
  - brain
  - cardiovascular
Preeclampsia:
increased future maternal cardiovascular risk

- **Irgens HU et al, BMJ 2001**
  *Preterm PE*: risk of death from: CVD 8↑
  stroke 5↑

- **Smith GC et al, Lancet 2001**
  *PE*: risk for CVD 2↑
  *PE and <2.5 kg baby*: risk for CVD 7↑

- **Bellamy L et al (Williams D), BMJ 2007**
  *PE > 10 years*: 4↑ risk for hypertension
  2↑ risk for ischemic heart disease/stroke

- **Lykke JA et al, Hypertension 2009**
  *PE*: ↑ risk for hypertension (PE severity-dependent)
Pathogenesis of preeclampsia

Unknown

➢ "Disease of theories"

- anti-angiogenesis
- microvascular damage
Engraved plaques at the Chicago Lying-in Hospital

” ... reserved for the scientist who discovers the cause and cure of preeclampsia. ......”

It is still blank today ......
.. it is somehow linked to the placenta
Redefining Preeclampsia

Hypertension

Redefining Preeclampsia Using Placenta-Derived Biomarkers
Anne Cathrine Staff, Samantha J. Benton, Peter von Dadelszen, James M. Roberts, Robert N. Taylor, Robert W. Powers, D. Stephen Charnock-Jones and Christopher W.G. Redman
+ sFlt-1/PIGF
WHAT ARE PREGNANT WOMEN DYING FROM?

- Pre-existing medical conditions exacerbated by pregnancy (such as diabetes, malaria, HIV, obesity): 28%
- Severe bleeding: 27%
- Pregnancy-induced high blood pressure: 14%
- Infections (mostly after childbirth): 11%
- Blood clots: 3%
- Abortion complications: 8%
- Obstructed labour and other direct causes: 9%
Global burden of Preeclampsia

2010 data

• WHO estimates that worldwide, and on a daily basis, up to 800 women die due to pregnancy and birth-related complications that potentially could have been prevented

• Preeclampsia is the third leading cause of maternal death - and is one of the major causes of preterm birth - and fetal morbidity and mortality

..... ≈ 100 women die of PE

..........every day
Maternal Mortality Rates – WHO 2010
EARLY DETECTION Saves Lives
• An utopic, yet possible scenario:
  - by using our smart phones we record a short video of some regions of interest (ROI) in our body (e.g. our face or our tongue)

• By using artificial intelligence (AI) transforming this ordinary smart phone into an ingenious equipment for detecting, predicting or even staging disorders –

  such as preeclampsia
By examining subtle changes such as motions, colors and deformations invisible to the naked eye, we could unveil hidden, but crucial, health information. 

...will this pregnant woman later develop manifest PE...?
The AI technology

Input video

Spatial Decomposition

Temporal Processing (pixel-wise)

Eulerian video magnification

Reconstruction

Output video
The main steps of video processing technology (ref. E. Nadimi):

- Firstly decomposing the input video sequence into a sequence of frames, where each frame is an image.

- In the first layer, each image goes through decomposition into different spatial frequency bands.

- The spatial decomposition is a filter that blurs the image at different degrees.
• In the second layer, the method applies a temporal filter to all bands. This temporal filter and its lower frequency and higher frequency limit, will depend on the specific application.

• The filtered spatial bands are then amplified by a given factor, and added back to the original signal

• The fourth layer is a spatial composition, in which the image is reconstructed by the composition of the enhanced images, to generate the final output video.

The main steps

video processing technology ref. E Nadimi
The final goal:

• **prevent** consequences of PE

• **provide a feasible** and cost effective **mobile health tool**

• **allowing automatic and continuous risk assessment** of PE-related pregnancy complications.
Videocamera/ smartphone project - Preeclampsia

• Case/control study based on believed pathophysiology of pre-eclampsia

• Recordings of pregnant women's faces 3 times during pregnancy

• Changes in colors of micropixel measured over time

• Inflammation in microvessels → increased ”redness” in the skin

• Will this increased redness be present before onset of clinical symptoms?
Eye movements

Colour changes in skin

Colour changes on tongue
Don’t give up!
Extra Slides
Progress and Results (beforehand from diabetes patients)

1. Designing the experimental setup

Facial redness and its variation
Head movements
Saccades
Smooth pursuit movements

Fokuser på det hvide punkt og følg punktet med dine øjne så præcist som muligt. Prøv at undgå at flytte hovedet så meget som muligt.
Progress (beforehand from diabetes patients)

3. Quantitative feature extraction and analysis

3.1. Revealing invisible facial color changes

- The facial redness appears to be higher in diabetic patients (even in those diabetic patients in which Rubeosis Faciei is not evident)
- The variation in facial redness appears to be higher in diabetic patients.
- The facial redness appears to be normally distributed in diabetic patients.
Progress (beforehand from diabetes patients)

3. Quantitative feature extraction and analysis

3.2. Metrics of the saccadic eye movements

3.3. Pulse detection from magnification of head movements

![Diagram of saccadic eye movements and pulse detection from head movements](image)
AI applied to screening for Diabetic Retinopathy

RETIPROGRAM

Dr. Aida Valls-Mateu
Doctor in Artificial Intelligence
Engineer in Computer Science
Associate professor at Universitat Rovira i Virgili (Tarragona, Catalonia)
Head of ITAKA research group  aida.valls@urv.cat

Work done in collaboration with Hospital Universitari Sant Joan de Reus
Head Ophthalmology: Dr. Pere Romero-Aroca promero@grupsagessa.com
Diabetic retinopathy (DR) is a health problem that affects many people and whose incidence is increasing:

- 415 millions of adults with diabetes in the world
- Increase of 50% until 2025
- 35% - 50% of diabetic people may have DR
- 10% in risk of becoming blind due to DR = This is about 20 millions of people

http://www.idf.org

South of Catalonia study:
Hospital Universitario Sant Joan (HUSJ):

- Reference population: 247.174
- Patients with diabetes mellitus: 17.792
- Health care centers: 15
- Non midryatic cameras for DR detection: 4 (since 2007)
Fig. 1. Prevention strategies for tackling the epidemic of diabetic retinopathy. DR, diabetic retinopathy; DME, diabetic macular edema; VI, visual impairments; M, 1 million people.

Wong TY, Sabanayagam C. Strategies to Tackle the Global Burden of Diabetic Retinopathy: From Epidemiology to Artificial Intelligence. Ophthalmologica, 2019 DOI: 10.1159/000502387
Both systems have been constructed using Machine Learning techniques from AI:

- **Retiprogram** uses Fuzzy Random Forests to build a set of rules with linguistic variables.
- **Image classification** model is constructed with Deep Learning techniques based on neural networks.
- In both cases the learning algorithm needs a large set of labelled training data to build the model. This model is validated with a different dataset of testing data, also labelled.

This work has been possible thanks to 3 Funded Projects by Instituto de Investigación Sanitaria Carlos III and FEDER funds.
PATIENT Diabetes Mellitus
Health Care
Regular control visit

FAMILY DOCTOR
Clinical Data from EHR

Calculate risk of developing DR

TEST
Obtain an eye fundus image with a non-midryatic camera

OPHTALMOLOGIST
Confirmation, diagnosis and treatment

No risk or low risk. Schedule next visit with the doctor

No risk or low risk. Schedule next visit with the doctor

Moderate risk or uncertainty

Moderate risk or uncertainty

The image is included in the calculation of risk of DR
The model uses 9 risk factors from EHR: age, treatment type, body mass index, creatinine, etc.

Random forest model has 200 trees, with an average of 80 rules on each tree.

Each rules uses around 3 to 7 of the risk factors.
Examples of fuzzy rules:

- IF Evol is short and HTAR with good control and BMI is normal_low THEN riskDR=NO
- IF Evol is short and HTAR with bad control and CKDEPI is low and Age is Old THEN riskDR=Yes
- IF Evol is very_long and BMI is obese_high THEN riskDR=Yes

AI applied to screening of Diabetic Retinopathy
We obtain Specificity around 85% and Sensitivity around 80%.
False Positives are much higher than False Negatives.

15000 patients from HUSJ

<table>
<thead>
<tr>
<th></th>
<th>11000</th>
<th>4000</th>
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<tbody>
<tr>
<td>Training</td>
<td></td>
<td></td>
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<tr>
<td>Testing</td>
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Validation with 28000 patients from other Catalan population
Validation with 108000 patients from Catalonia population (2018)
ONGOING Use in a pilot test at HJSU (Reus)
Wong TY, Sabanayagam C. Strategies to Tackle the Global Burden of Diabetic Retinopathy: From Epidemiology to Artificial Intelligence. Ophthalmologica, 2019 DOI: 10.1159/000502387
Deep Learning for Image Classification

Model constructed with EyePACS dataset

Validation and re-training with Messidor-2 dataset
• Important difference with other Deep Learning models (i.e. Google): we are able to **classify into 4 different classes**. Others only binary classification (YES/NO)

• Results of the validation with images HUSJ data: 5.122 images

<table>
<thead>
<tr>
<th>Model Classification</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Ophthalmologists Classification</td>
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<td>54</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
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<td>110</td>
<td>47</td>
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<tr>
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<tr>
<td>2</td>
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</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NO retinop</strong></td>
<td>4322</td>
<td></td>
<td></td>
<td>66</td>
</tr>
<tr>
<td><strong>YES retinop</strong></td>
<td>78</td>
<td></td>
<td>534</td>
<td></td>
</tr>
</tbody>
</table>
• The system developed is able to display the pixels that have been used by the model to make the classification.
• We are studying the relation between these pixels and the eye lesions.
  Example with class 1: mild Retinopathy
• The system developed is able to display the pixels that have been used by the model to make the classification.
• We are studying the relation between these pixels and the eye lesions.

Example with class 3: severe Retinopathy
AI applied to screening of Diabetic Retinopathy

**Model 1:** Image Classification in 5 levels of DR

**Model 2:** Detection if an image is good/bad

**Automatic Image Classification**

**Fig. 1.** Prevention strategies for tackling the epidemic of diabetic retinopathy. DR, diabetic retinopathy; DME, diabetic macular edema; VI, visual impairments; M, 1 million people.

*Wong TY, Sabanayagam C. Strategies to Tackle the Global Burden of Diabetic Retinopathy: From Epidemiology to Artificial Intelligence. Ophthalmologica, 2019 DOI: 10.1159/000502387*
Learning for Image Classification

Is the image good enough to detect DR?
Current work:
1. Extract indicators from the images to be included in Retiprogram.
2. We are exploring the possibility of developing an online self-assessment system for image reading and classification.
AI applied to screening of Diabetic Retinopathy

Dr. Aida Valls-Mateu
URV, ITAKA research group  aida.valls@urv.cat

Dr. Pere Romero-Aroca
IISPV, Hospital Universitari Sant Joan de Reus  promero@grupsagessa.com

Publicacions:


Artificial Intelligence for Diagnosis and Treatment in Dermatology

Marc Combalia Escudero
Hospital Clínic de Barcelona
List of contents

1. Why skin cancer?

2. Artificial Intelligence for Skin Cancer Diagnosis
   1. ISIC Collaboration
   2. ISIC Challenge 2019
   3. ISIC Reader Study

3. Artificial Intelligence for Treatment Recommendation
1. Why skin cancer?
1.1. Why skin cancer?

- Skin
  - Largest organ of the human body
- Main entry barrier
- Temperature regulation
- Cutaneous sensibility
- …
1.2. Why skin cancer?

- Skin cancer
- Uncontrolled growth of abnormal skin cells
- Most diagnosed cancer in the US
- Increasing incidence rates in all the age ranges
1.3. Why skin cancer?

- Skin cancer can be diagnosed via visual inspection.
- Skin cancer is easy to treat (most times excision of the lesion suffices) if detected early.
- Great opportunity for artificial intelligence.
2. Artificial Intelligence for Skin Cancer Diagnosis
2.1. Our collaboration with ISIC
(International Skin Imaging Collaboration)
2.2. ISIC 2019 Challenge

Is artificial intelligence prepared for the clinical reality?
ISIC 2019
Skin Lesion Analysis Towards Melanoma Detection

Background
Skin cancer is the most common cancer globally, with melanoma being the most deadly form. Dermoscopy is a skin imaging modality that has demonstrated improvement for diagnosis of skin cancer compared to unaided visual inspection. However, clinicians should receive adequate training for those improvements to be realized. In order to make expertise more widely available, the International Skin Imaging Collaboration (ISIC) has developed the ISIC Archive, an international repository of dermoscopic images, for both the purposes of clinical training, and for supporting technical research toward automated algorithmic analysis by hosting the ISIC Challenges.

Task
The goal for ISIC 2019 is classify dermoscopic images among nine different diagnostic categories:
1. Melanoma
2. Melanocytic nevus
3. Basal cell carcinoma
4. Actinic keratosis
5. Benign keratosis (solar lentigo / seborrheic keratosis / lichen planus-like keratosis)
6. Dermatofibroma
7. Vascular lesion
8. Squamous cell carcinoma
Data Descriptor: The HAM10000 dataset, a large collection of multi-source dermatoscopy images of skin lesions.

BCN20000: DERMOSCOPIC LESIONS IN THE WILD

A PREPRINT

Marc Combalia¹, Noel C. F. Coderella², Veronica Rotemberg³, Brian Helba⁴, Veronica Vilaplana⁵, Ofer Reiter⁶, Cristina Carrera⁷, Alicia Barreiro⁸, Allan C. Halpern⁹, Susana Puig⁵, and Josep Malvehy⁷

¹Melanoma Unit, Dermatology Department, Hospital Clinic Barcelona, Universitat de Barcelona, IDIBAPS, Barcelona, Spain
²IBM Research AI, T J Watson Research Center, Yorktown Heights, NY, USA
³Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
⁴Kitware, Clifton Park, NY, USA
⁵Signal Theory and Communications, Universitat Politècnica de Catalunya, Barcelona, Spain

ABSTRACT

This article summarizes the BCN20000 dataset, composed of 19424 dermoscopic images of skin lesions captured from 2010 to 2016 in the facilities of the Hospital Clinic in Barcelona. With this dataset, we aim to study the problem of unconstrained classification of dermoscopic images of skin cancer, including lesions found in hard-to-diagnose locations (nails and mucosa), large lesions which do not fit in the aperture of the dermoscopy device, and hypo-pigmented lesions. The BCN20000 will be provided to the participants of the ISIC Challenge 2019 [8], where they will be asked to train algorithms to classify dermoscopic images of skin cancer automatically.
ISIC Challenge 2019
Task Overview

- Skin lesion classification
- Unfiltered lesions
  - Non-Pigmented lesions
  - Uncommon anatomic locations
  - Large lesions
  - Ulcerated lesions
  - Out of distribution lesions
- Metadata around patients
2.3. ISIC Challenge 2019 Reader Study
3. Artificial Intelligence for Skin Cancer Risk Assessment
Lifelines

- Mortality and Relapse data
  - Very hard to obtain
- Patient features
  - Genetic features
  - Tumor features
  - Imaging features
  - Blood analyses
- Treatment features
  - Treatment over time
Artificial Intelligence is going to be a Key Player in the Medicine of the Near Future
Deep Lung – Lung Cancer Detection with Deep Learning
EHTEL Symposium 2019

Xavier Rafael, Giuseppe Pezzano, Ilaria Bonavita, Paula Subías, Anton Aubanell MD, Esther Pallissa MD, Oscar Persiva MD, Miguel Ángel González PhD, Laura Ruiz PhD, Carles Rubies, Eduard Monsó MD PhD, Xavier Gallardo MD PhD, Vicent Ribas PhD.
Objectives

- According to the American Cancer Society, Lung Cancer (LC) is the second most common cancer and the most lethal. LC kills more people than colon, prostate and breast cancers all together.
- **Deep Lung** aims at providing automatic analyses of medical images through Deep Learning techniques to improve the detection of LC.
- The project develops three tools:
  - Study of thorax RX for the incidental detection of lung masses.
  - Study of CT scans for nodule detection
  - Segmentation of lung nodules and study their malignancy.
- The project is validated through two clinical studies at Hospital Vall d’Hebron (CT) and Hospital Parc Taulí (RX).
Mass detection from RX

**GOAL:** improve nodule detection on X-ray thorax images, in order to reduce radiologists amount of work and helping to an early treatment of the disease.
Mass detection from RX

1st classifier
Frontal Thorax?

- Classifier using convolutional networks (ResNet-50)
- Results:
  - Accuracy: 99%

2nd classifier
Nodule?

- Data: 2200 images
  - (600 positive + 1600 controls)
- Classifier with convolutional networks 2D (ResNet-34*)
- Results:
  - Accuracy: 78%
  - Sensitivity: 76%
  - Specificity: 79%
Mass detection from RX

Test on 24685 unlabeled images

- Mean time per image:
  - Classifier I: 0.63 s
  - Classifier II: 0.45 s
Need: Improve the predictive capability and reduce the radiologist’s workload in the detection of lung nodules (>=6 mm, <3 cm) and assess their growth over time.
Nodule detection from CT Scans

Total anonymized cases:
170 CT-pairs (>500K slices)
113 Cancer/57 Bening

Clinical data:
Age
Gender
Smoker or former smoker
Drinker or former drinker
Previous Neoplasms
Exitus

Annotations:
Diameter
Type cancer
Type nodule
Malignancy (0/1 cancer)
Nodule detection from CT Scans

Experiment
- 3D Faster-RCNN [2]
- Does not require segmentation of lung tissue
- Input 128 | Output 32,3,5
- 3 anchor sizes (5,10,20)

Data:
- LIDC/IDRI dataset
- ~ 900 CTs
- ~ 1200 labelled nodules
- Annotation (4 radiologists)
- Nodules >=3 mm
- N providers (e.g. Siemens)
- M resolutions (<5mm)

Resultats
- Avg FROC: 0.8084

Nodule segmentation

**Experiment**

- Axial segmentation of nodules (2D)
  - Methods:
    - U-net adapted
    - Data augmentation
    - Transfer learning,…
  - Input: 512x512x3
  - 3 consecutive axial cuts + mask
  - Output: Mask (nodule/no nodule)

**Data:**

LIDC/IDRI dataset

~ 900 CTs
~ 1200 segmented nodules
Annotations (4 radiologists)
Nodules>=3 mm
N providers (e.g. Siemens)
M resolutions (<5mm)

**Results**

- Test on 104 cases

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Nodule segmentation

Experiment

- **3D segmentation in cubes**
- Methods:
  - 3D U-net
  - Data Augmentation
- Input: 64x64x64 + 3D nodule masks
- Output: 3D Pixel-wise mask predictions

Results
Conclusions

• The project is being validated in two clinical studies and a pilot (Hospital Vall d’Hebron and Parc Taulí).
• The potential of the project lies in the fact that it takes into consideration the temporal evolution of nodules.
• The project is aligned with the radiology workflow and, therefore, may represent an improvement on the efficiency of this process and productivity.
Deep Lung
Moltes gràcies!
¡Muchas gracias!
Thank you!
Grazie!
Merci!
Tack!

vicent.ribas@eurecat.org