A Medical Decision Support System for Explainable Multimodal Detection of Non-Small Cell Lung Cancer Using Clinical and PET Data

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- Medical Doctor/Specialist in Nuclear Medicine, School of Medicine, University of Patras, Patras, Greece
- Hold a PhD in Medicine from the University of Patras (Dec. 2010) and specialization in Nuclear Medicine, School of Medicine, Nuclear Medicine Clinical Lab, University Hospital of Patras (Rio), Greece (2009).
- Specialize in nuclear medical diagnosis, nuclear imaging, medical decision support systems, AI applications in nuclear medicine, medical informatics, applications of ionizing radiation in medicine etc.
- More than 80 publications in journals, conference papers and book chapters and has more than **1000** citations from independent researchers (**h-index=18 in GoogleScholar**).
- EMERALD project: Faculty member for the development of new AI and XAI decision-making models in Nuclear Medical Diagnosis.
- Supervisor in the following **Github** open-source libraries:

  XAI-ML library: https://github.com/emeraldUTH/EMERALD

  pyXAI-FCM library in Medical Diagnosis: https://github.com/npapandrianos/pyXAI-FCM

  pyXAI-NuclearMed: https://github.com/npapandrianos/pyXAI-NuclearMed

Motivation

- In healthcare, the majority of applications are black boxes
- Lack of transparency/explainability in black box models like ML, DL
- Importance of explainable models in medical diagnosis
- Critical - Advanced soft computing methods with explainable features

Statement of the problem

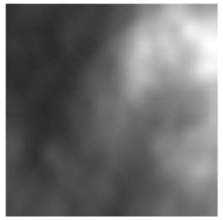
Non-Small Cell Lung Cancer (NSCLC)

- Most common form of lung cancer (85% of all lung cancer cases)
- Early diagnosis: Solitary Pulmonary Nodules' (SPNs) malignancy detection

❑ Increased demand for PET imaging in nuclear medicine diminishing the number of available physicians, making mandatory the <u>use of automated diagnostic frameworks</u>

❑ Early and accurate diagnosis is crucial to improve patient outcomes and reduce mortality rates (NSCLC is a life-threatening disease).

Benign Case



Malignant Case

In the field of NSCLC, ML and DL methods have been used extensively for diagnostic classification, often functioning as black-box models. Consequently, developing *explainable* models presents a critical challenge for transparent and reliable NSCLC

Objectives

- To develop explainable models for transparent and reliable NSCLC diagnosis, using both PET images and clinical risk factors.
- To enhance the recently proposed DeepFCM, for automatic classification and diagnosis of NSCLC in nuclear oncology, producing more interpretable predictions in the task of decision making.
- To employ Natural Language Generation (NLG) to transform DeepFCM results into human-readable explanations

Data Description

- ➢ PET (Positron Emission Tomography) images
- ➢ 9 clinical characteristics

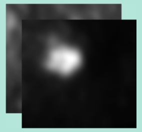
PET/CT data were collected using a Discovery iQ3 sl16 scanner with a 15cm field of view, reconstructing 35 axial images at 4.25mm intervals. Patients were scanned in a supine position to capture 3D volumes using multiple bed positions.

Info about dataset

Dataset obtained	2018-2022
Instances	456
Malignant	234
Benign	222
Male	32.24%
Female	67.76%
Age range	43-87

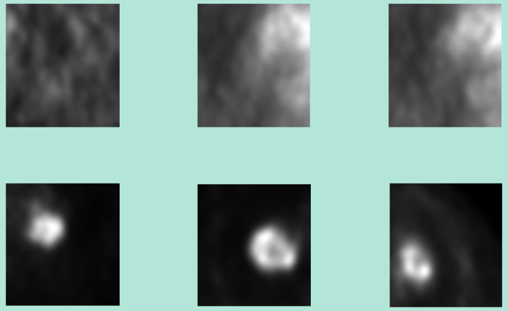
Dataset

456 Total cases



222 Benign Cases

234 Malignant Cases



9 Clinical Characteristics (Gender, Age, BMI, SUV, GLU, Diameter, Location, Type, Margins)

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EMERALD's Challenge

The challenge

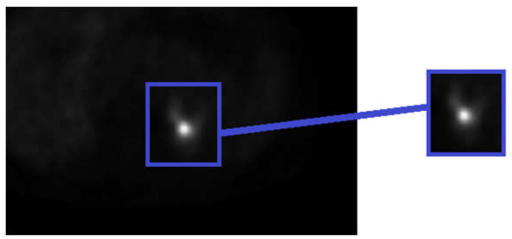
Predict the malignancy of Solitary Pulmonary Nodules (SPNs) using multiple input features (PET image, SPN characteristics) – multimodal diagnosis

DeepFCM with two learning methods, PSO and GA are used

Patient Demographic info and SPN characteristics

A/A	Feature Name	Description	Feature Class/Type
1	Gender	Male/female	Demographics
2	Age	Years of age of the patient	Demographics
3	BMI	Body Mass Index	Demographics
4	SUV	SUV max index	Medical index
5	GLU	Glycemic Load index	Medical index
6	Diameter	Diameter of SPN	Positional Data
7	Location	Location of SPN	Positional Data
8	Type	Type	SPNs morphology data
9	Margins	Margins of SPN	Positional Data
10	Benign/Malignant	Class (as diagnosed by the medical expert)	Reference Variable

SPN in PET Image



The Region of Interest (ROI) is cropped to focus on the relevant area for analysis, enhancing the accuracy of model predictions by isolating critical features.

Why to explore DeepFCM for NSCLC Diagnosis?

DeepFCM is a multimodal approach that handles clinical and imaging data and combines:

- The transparent representation of influence among concepts of Fuzzy Cognitive Maps (FCM)
- The feature extraction capabilities of Convolutional Neural Networks (CNNs).

MDSS

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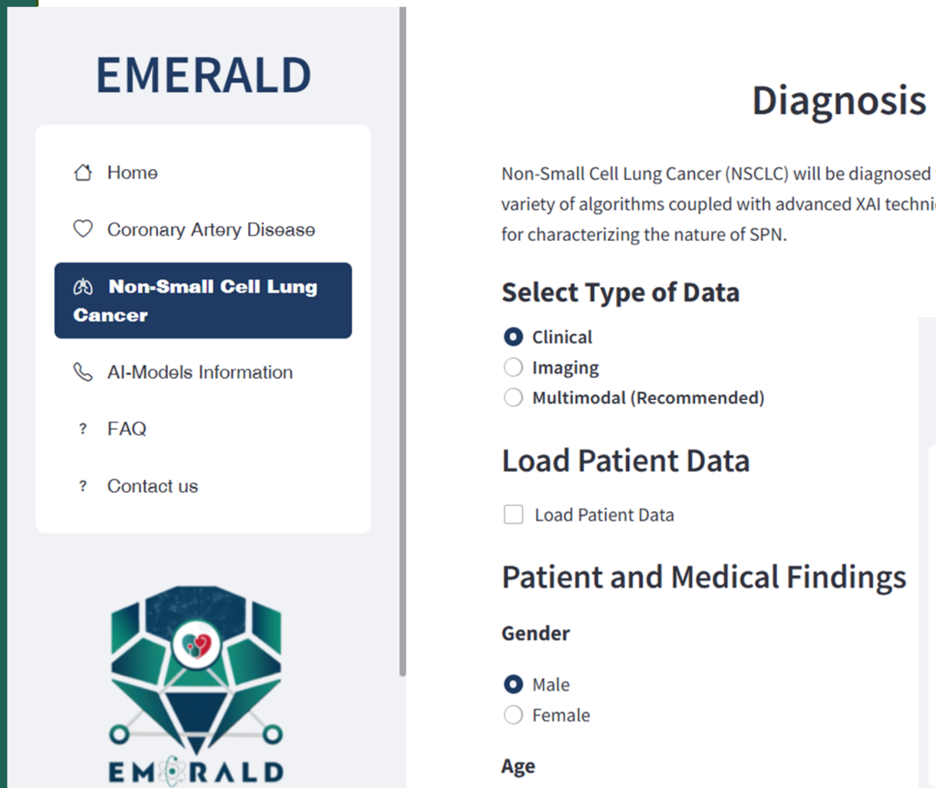
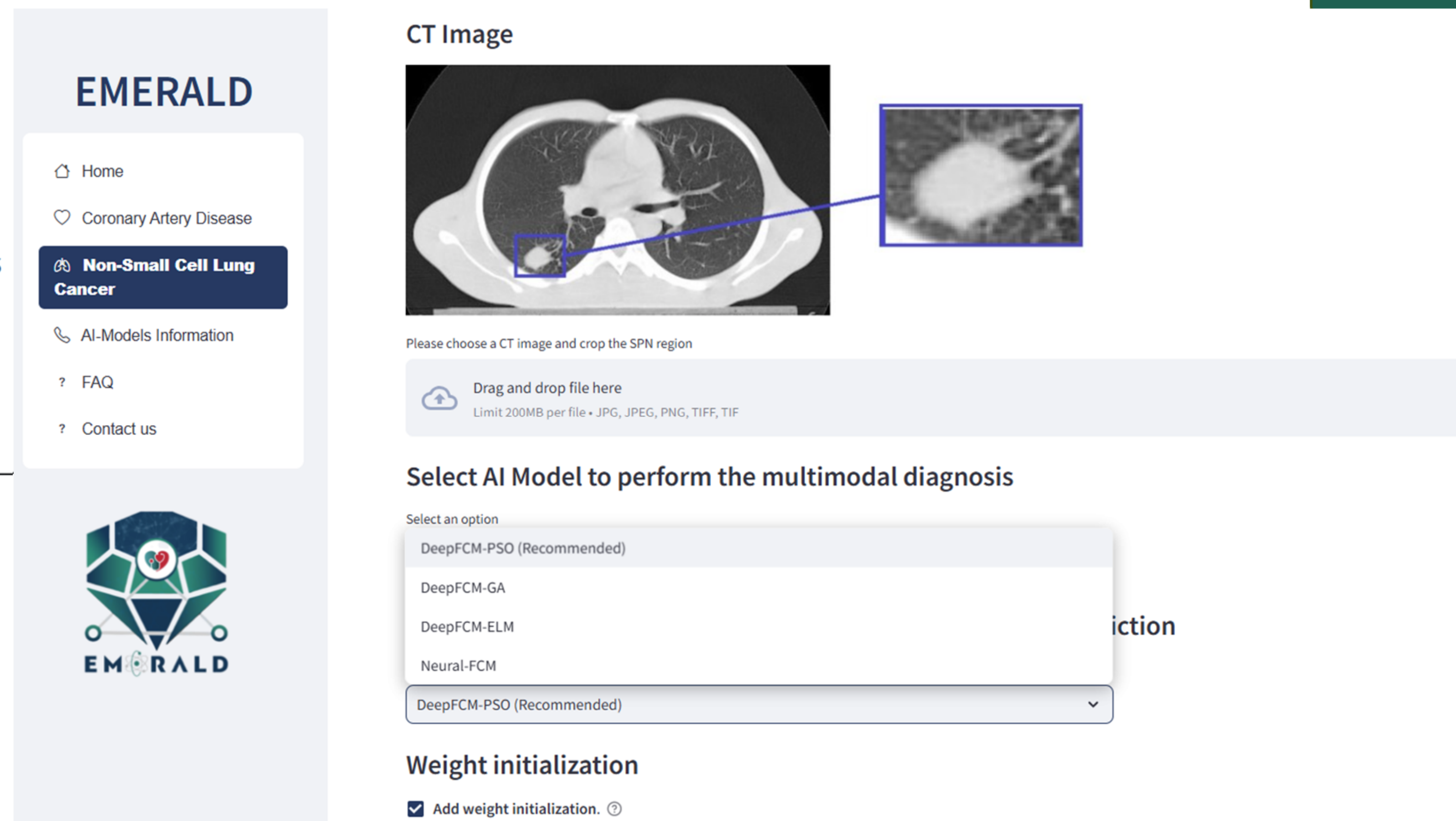
MDSS

DeepFCM is incorporated into a Medical Decision Support System (MDSS) developed by the EMERALD team.





DeepFCM Workflow

STEP 1

Multimodal Dataset

Clinical data serve as FCM input concepts, while RGB-CNN, trained on images, generates predictions that are combined with clinical data to construct the multimodal dataset.

STEP 2

Calculation of Interconnections

Experts provide in the form of fuzzy sets, the initial concept relationships, while PSO and GA are employed in training DeepFCM, refining the interconnections among concepts.

STEP 3

DeepFCM Construction

DeepFCM establishes interconnections between input and output concepts, providing a transparent view of how each clinical and imaging factor impacts the final diagnosis.

STEP 4

Gradient-Class Activation Mapping

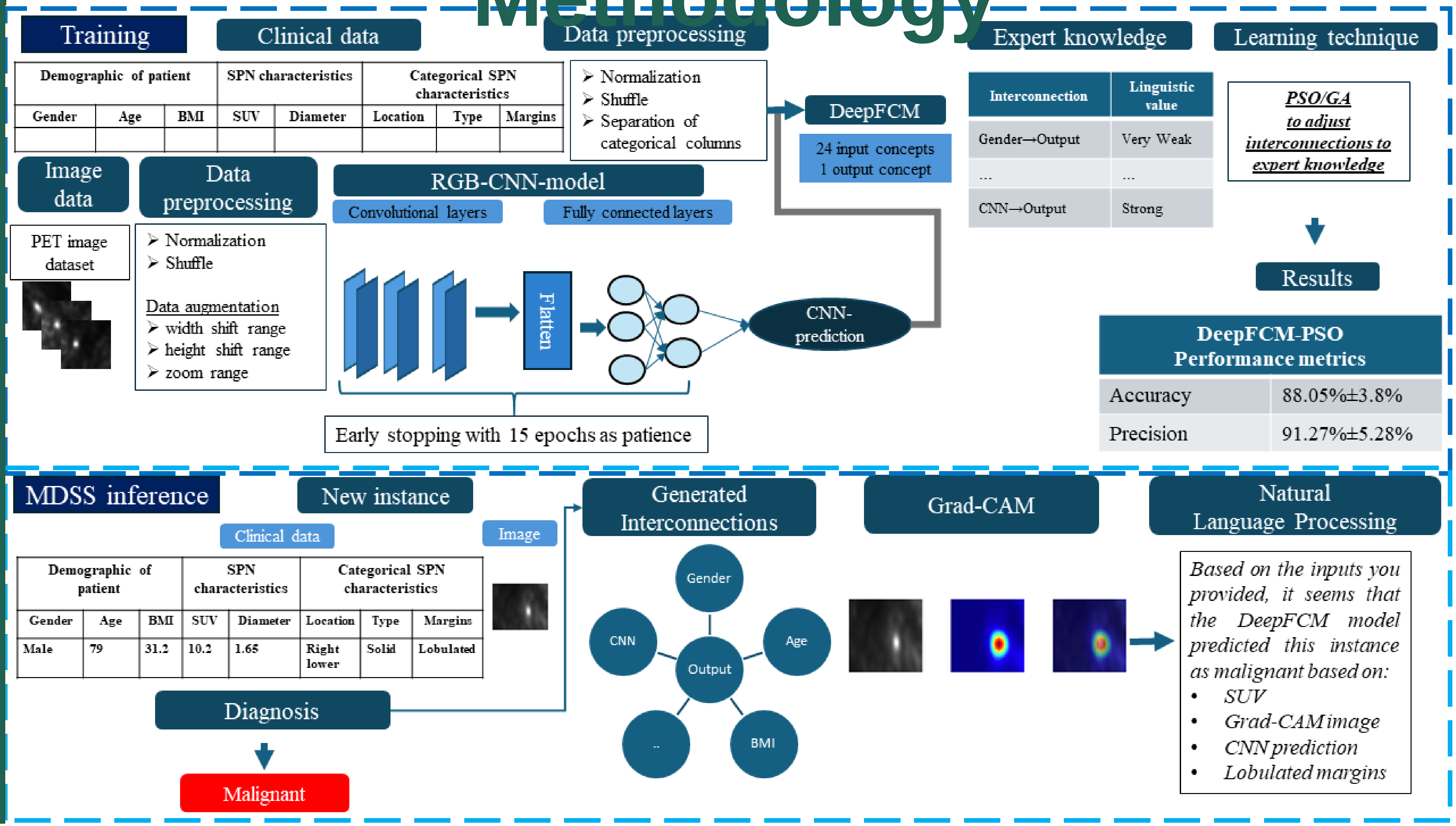
Grad-CAM highlights specific regions within medical images by leveraging feature maps generated by the RGB-CNN, pinpointing areas that strongly influence the model's prediction.

STEP 5

Natural Language Generation

Through NLG, DeepFCM results are translated into human-readable explanations, enhancing interpretability and clinical relevance.

DeepFCM-based Methodology



Two learning techniques for DeepFCM

Particle Swarm Optimization (PSO) - DeepFCM-PSO

- Deploys a swarm of particles, each representing a potential solution (weight matrix of concept interconnections), to enhance the model iteratively.

Key Parameters Modifications

- Number of particles
- Constant inertia weight
- Cognitive constant
- Social constant

Methods

1. Evaluate particle()
2. Update velocity()
3. Update position()

Genetic Algorithm (GA) –DeepFCM-GA

- Utilizes evolutionary strategies such as selection, crossover, and mutation to optimize relationships between concepts.

Key Parameters Modifications

- Number of population
- Number of generations
- Crossover rate
- Mutation rate

Methods

1. Selection()
2. Crossover()
3. Mutation()
4. Evaluate fitness function()

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Performance metrics across models

Model	Accuracy	Loss	Sensitivity	Specificity	Precision
RGB-CNN	83.12%±6.43%	0.3	92.26%±6.18%	91.91%±9.21%	91.31%±5.75%
DeepFCM-PSO	**88.14%±3.8%**	**0.12**	**88.36%±5.23%**	**87.29%±7.48%**	**91.27%±5.28%**
DeepFCM-GA	87.08%±5.96%	0.13	84.56%±12.29%	85.38%±6.83%	87.79%±6.16%
Kim et al. (2022) [4]	73.23%±6.0%	-	80.08%±6.4%	-	75.71%±4.8%
Apostolopoulos et al. (2024) [5]	85.21% (95% CI: 83.74%–86.68%)		81.23% (95% CI: 79.22%–83.24%)	95.37% (95% CI: 92.99%–97.75%)	85.21% (95% CI: 83.74%–86.68%)
Caruso et al. (2022) [6]	75%±16.2%	-	84%±15.17%	75%±16.2%	-

[4] G. Kim, S. Moon, and J.-H. Choi, “Deep Learning with Multimodal Integration for Predicting Recurrence in Patients with Non-Small Cell Lung Cancer,” Sensors (Basel), vol. 22, no. 17, p. 6594, Aug. 2022, doi: 10.3390/s22176594.
[5] I. D. Apostolopoulos, N. D. Papathanasiou, D. J. Apostolopoulos, N. Papandrianos, and E. I. Papageorgiou, “A Multi-Modal Machine Learning Methodology for Predicting Solitary Pulmonary Nodule Malignancy in Patients Undergoing PET/CT Examination,” Big Data and Cognitive Computing, Aug. 2024, doi 10.3390/bdcc8080085..
[6] C. M. Caruso et al., “A Multimodal Ensemble Driven by Multiobjective Optimisation to Predict Overall Survival in Non-Small-Cell Lung Cancer,” Journal of Imaging, vol. 8, no. 11, Art. no. 11, Nov. 2022, doi: 10.3390/jimaging8110298.

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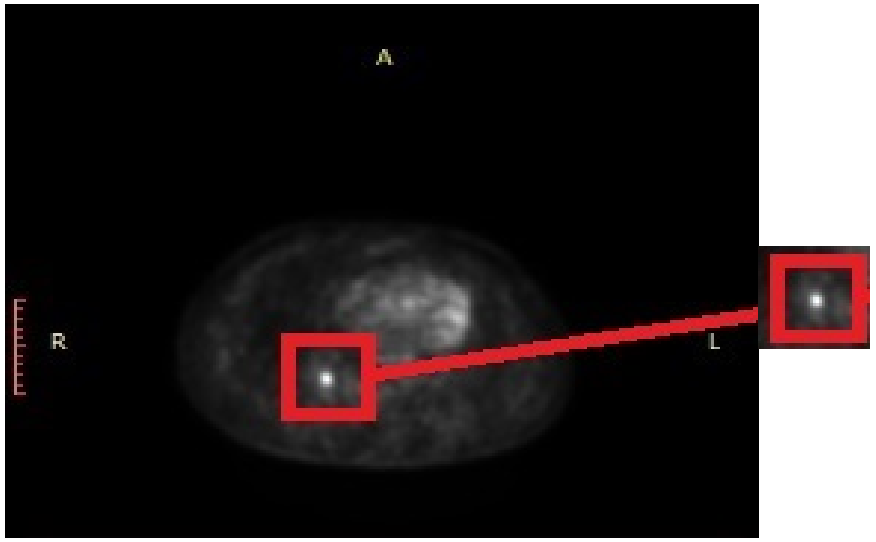
NSCLC case study

Patient's information and SPN Clinical characteristics

A/A	Feature Name	Value
1	Patient's age	63 years old
2	Gender	Male
3	BMI	27.8
4	GLU	89
5	SUV	10.2
6	Diameter	2.7 cm
7	Location	Right Lower Lobe
8	Type	Semi-Solid
9	Margins	Lobulated

SPN Representation in PET Image



NSCLC diagnosis using DeepFCM

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Decision: Malignant

The selected model exhibits the following evaluation metrics in **EMERALD external test patient cohorts:**

Accuracy: 88.14% **Sensitivity: 88.36%** **Specificity: 87.29%**

Explainability through the DeepFCM model

Linguistic values for interconnections among concepts

- **Very Weak**: Interconnection values in the range of [0-0.25].
- **Weak**: Interconnection values in the range of [0.1-0.4].
- **Medium**: Interconnection values in the range of [0.35-0.65].
- **Strong**: Interconnection values in the range of [0.55-0.85].
- **Very Strong**: Interconnection values in the range of [0.75-1].

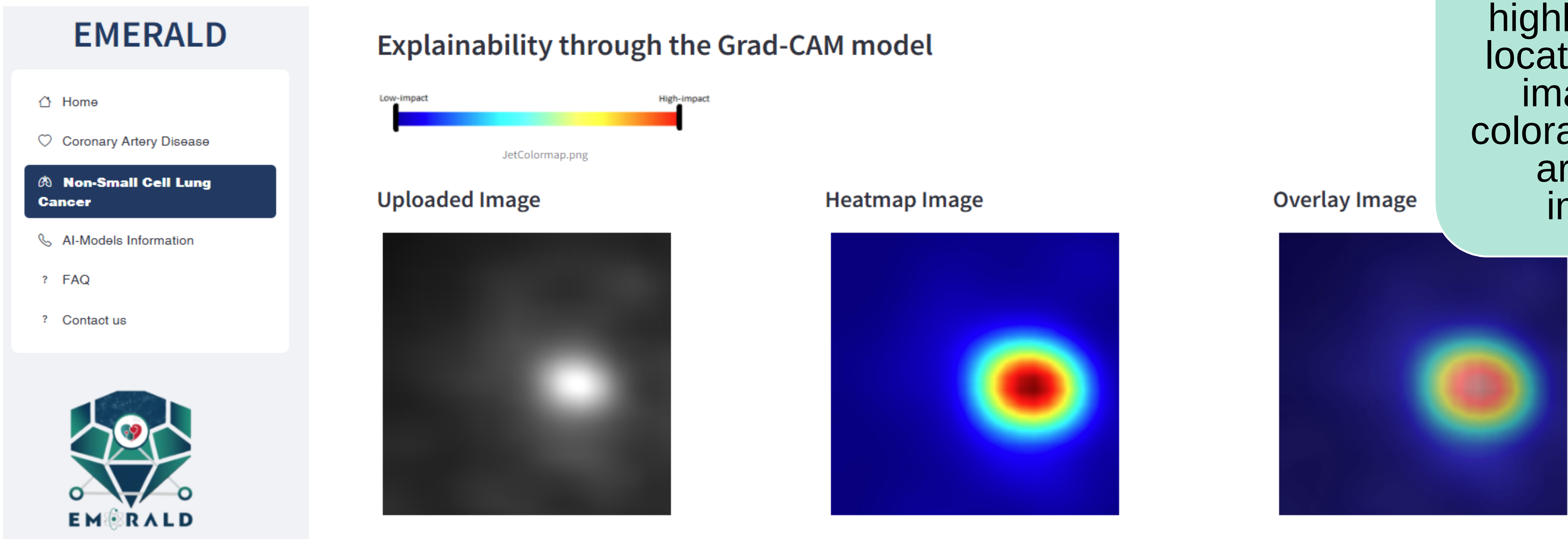
Edge Colors

- **Edges in Green and Red:**
  - **Green edges** indicate features that have a positive impact on the prediction.
  - **Red edges** indicate features that have a negative impact on the prediction.

DeepFCM-PSO classified this instance as **malignant**, identifying key interconnections between input factors and the outcome. The **SUVmax** and the **lobulated margins** of the SPN are the most influential features in this prediction.

Gradient-weighted Class Activation Mapping

Grad-CAM accurately highlights the SPN location in the PET image with red coloration, indicating areas of high importance.



1. **Uploaded Image (Cropped Region):** A zoomed-in section of the PET scan, focused on the ROI containing the SPN for precise analysis.
2. **Heatmap**: A visualization highlighting the areas in the image where the CNN model detected significant features related to malignancy risk.
3. **Overlay in Grad-CAM**: A combined image of the original scan and heatmap, displaying the highlighted regions directly on the SPN for enhanced interpretability of the model's prediction.

Natural Language Generation

Explanation through NLG reasoning

Conclusions:

The Deep Fuzzy Cognitive Map (DeepFCM) has concluded that the Solitary Pulmonary Nodule (SPN) in this case is malignant. This aligns with the Convolutional Neural Network (CNN) model's decision, which also indicated malignancy. The clinical values and image analyses collectively support this decision, with significant influence from specific clinical features and image regions.

Further Details:

- **Clinical Values:**
  - **Standardized Uptake Value (SUV):** This is the most significant clinical factor, with a very high influence on the outcome. The SUV of 10.2 is substantially elevated, indicating high metabolic activity typical of malignant nodules.
  - **Diameter:** The nodule's diameter of 2.7 cm is another critical factor, as larger nodules have a higher probability of being malignant.
  - **Margins (Lobulated):** The lobulated margins are a strong indicator of malignancy, contributing significantly to the decision.
  - **Type (Semi-Solid):** Semi-solid nodules are more likely to be malignant compared to purely solid or purely ground-glass nodules.
  - **Location (Right Lower Lobe):** While the location has a moderate influence, nodules in the lower lobes are often scrutinized more closely in clinical practice.
- **Image Analysis:**
  - **Original Image:** The SPN's characteristics, such as its size and margins, are consistent with malignant features. The nodule's appearance in the original image suggests irregularity and potential invasiveness.
  - **Grad-CAM Heatmap:** The heatmap highlights areas of high importance in red, which correspond to the regions of the nodule with the most significant features indicating malignancy. These regions likely show increased metabolic activity or irregular growth patterns, supporting the malignant classification.

In summary, the combination of elevated SUV, significant nodule diameter, lobulated margins, and the semi-solid nature of the nodule, along with the supporting image analysis, strongly suggests malignancy. This case does not require further investigation as both the CNN model and DeepFCM are in agreement.

NLG analysis provides an explanation supporting consistent interpretation for the nuclear doctor. The reasoning highlights the most critical regions across **clinical** and **imaging** factors.

Conclusions

- **Significant Healthcare Advancement:**
  - Develop and enhance MDSS with explainable AI techniques.
  - Multimodal diagnosis for NSCLC.
- **Explainability and Transparency:**
  - DeepFCM interconnections provide insights into the influence of each clinical and imaging factor on NSCLC diagnosis.
  - Incorporation of Grad-CAM to interpret CNN predictions.
  - NLG reasoning to transform DeepFCM results into human-readable explanations.
- Limitations:
  - Dataset limited from a single hospital.

Future Work:

❑ Involve integrating **state equations** for DeepFCM learning to cope with uncertainty in experts' knowledge and combine Fuzzy Logic and Language Models to propose a textual explainer.

Thank you for your attention

- Questions?

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Thank you for your time

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