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# Impact of quality, type and volume of data used by deep learning models in the analysis of medical images



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#### ABSTRACT

The need for time and attention given by the doctor to the patient, due to the increased volume of medical data to be interpreted and filtered for diagnostic and therapeutic purposes has encouraged the development of the option to support, constructively and effectively, deep learning (DL) models for applications in the interpretation of medical images. Imaging physicians combine data from different stages and medical experiences, as opposed to DL models that incorporate the same types and modes of artisanal features. Access to big-databased medical imaging can be considered a benefit to the performance of DL models in interpreting medical imaging but similar or superior performance has been achieved with small, multi-feature and well-categorized databases that have improved annotation and labelling. The major contribution of this paper is primarily to highlight the impact of data quality, type and volume used by deep learning models in medical image analysis accompanied by updated characterization of the components of the deep learning process from data to medical applications. Second, it describes the specific correlations between the components of the deep learning process. Finally, it presents problems and directions for future research.

## 1. Introduction

The medical data most used in medical practice are medical images and for this reason most deep learning algorithms have targeted this category of medical information for the realization of medical applications.

A large number of medical images are stored in open access databases have private databases of some ceding institutions. These medical images are filed in connection with imaging reports or medical video image reports and, along with language processing from natural images, they have a great contribution to image analysis [1]. Annotation and labelling of the medical image, representing data from doctors, used through methods of integration into deep learning models, consumes time and requires specialized knowledge.

The large volume of training data and properly labelled determines the performance of the deep learning modeling in the interpretation of medical images. Because manual image labelling requires time and specialized training, standardized, organized labelling has been used which has the risk of over-labelling with unnecessary information [2].

In the absence of a large amount of data, the problem of overassembly can be eliminated by adding abandonment. The deep learning model can have increased preformation in these conditions by optimizing a large number of hyper-parameters (size and number of filters, depth, learning rate, activation function, number of hidden layers, etc.) [3].

In medical image analysis the data types have a high variability and can be exemplified by image captures from different regions [4] different types of data included in a phase [5], different types of images [6], data from doctors that has errors and requires time for processing [7], small sample sizes [8].

This paper presents a methodical review of the literature with the objective of carrying out an analysis of the importance of the

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relationship between the types and characteristics of scientific data and their use of deep learning models in the interpretation of medical images. We have defined a methodology for semi-automating the production of relevant articles and eliminating those with low impact in the scientific community, by applying inclusive and exclusive quality criteria in the fields of medicine and information technology.

The major contribution of this paper is primarily to highlight the impact of data quality, type and volume used by deep learning models in medical image analysis accompanied by updated characterization of the components of the deep learning process from data to medical applications. Second, it describes the specific correlations between the components of the deep learning process. Finally, it presents problems and directions for future research.

#### 2. State of the arts

The current state of performance of deep learning (DL) models and architectures depends on the nature and quality of the data used in their training. This section shows the data types and DL model description and classification according to medical data types used, objectives and performances in medical applications.

#### 2.1. Scientific data and dataset

Artificial neural networks are universal approximations: a relationship between inputs and outputs can be obtained (a model) with a performance that depends on data sets, topologies, training process, etc., being possible to obtain models for any medical information, such as be medical images. Current medical systems are unable to provide information on huge data sets due to limited laws or medical systems. DL models are just correlations of complex formulas between inputs (example: pixels) and outputs (example: disease labels). There is no semantics in a DL classifier for medical images (the model is not an understanding of medical concepts, but only a matrix of numbers. For this reason, it is not possible for DL to replace a doctor, it is just a tool, similar to the old computer assisted diagnostic (CAD) with predefined rules. There is also no federal intrusion and this involves limiting access to medical data due to inefficient systems and can be avoided, for example, by moving models from one center to another, the images will remain in the property center and patient privacy will be protected [9].

Access to big-databased medical imaging can be considered a benefit to the performance of DL models in interpreting medical imaging but similar or superior performance has been achieved with small, multifeature and well-categorized databases that have improved annotation and labelling.

Big-databased medical imaging requires the following interventions to improve their quality:

- Stratification of data according to certain characteristics,
- Identifying data with low occurrence in databases and eliminating it to avoid introducing "noise" and destabilize the algoritm
- Segmentation of similar data containing extensions (e.g., gender, age, etc.) by creating sub-segments,
- Segmentation of data to define the area of interest, elimination of variations specific to a feature to avoid the data "noise" of the algorithm, annotation of data that requires effort and time from doctors,
- Data labelling.

There are many large-scale and well-annotated data sets, such as ImageNet 1 (over 14 million images tagged in 20 k categories) and COCO 2 (with over 200 images annotated in 80 categories), medical datasets (open source), such as ChestX-ray14 and Deep-Lesion containing medical images tagged over 100k, the others, contain only a few thousands or even hundreds of medical images, and medical applications have developed properly in the medical fields.

The knowledge of experienced clinical-imaging physicians (radiologists, ophthalmologists and dermatologists, etc.) follows certain characteristics in images, namely, contrast, color, appearance, topology, shape, edges, etc., help and are used by deep learning models to perform the main tasks of medical image analysis [9],10].

The type and volume of medical data, the labels, the category of field knowledge and the methods of their integration into the DL architectures implicitly determine their performance in medical applications [9].

CT, PET-CT, MRI, X-rays, Ultrasound, Diagnostic Biopsy, Mammography and Spectrography are the most used imaging and exploratory investigations in the process of image interpretation, in the objective of extracting characteristics reducing or enlarging the size, in the group, segmentation and classification of images and by using integration methods contribute to the performance of deep learning models, see Fig. 1 [9–12].

Larger datasets, compared to the small size of many medical datasets, result in better deep learning models [4]. The large and well-annotated data sets are: ImageNet, COCO 2, (open source) medical data sets, see Fig. 2.

Acronyms: MRI Magnetic Resonance Images, CT Computed Tomography, SLO Scanning Laser Ophthalmoscopy images, The Alzheimer's disease neuroimaging initiative (ADNI), Automated cardiac diagnosis challenge (ACDC), The autism brain imaging data exchange (ABIDE), Automated Gleason grading of Prostate cancer tissue-histology images (AGPH) [13], Grand challenge on Breast Cancer Histology images (BACH) [14], Hospital-scale chest x-ray database and benchmarks on weakly-supervised classification and localization of common thorax diseases (Chestx-ray14), The lung image database consortium (LIDC) and image database resource initiative (IDRI) (LIDC-IDRI), Algorithms for automatic detection of pulmonary nodules in computed tomography images (LUNA16), Large dataset for abnormality detection in musculoskeletal radiographs (MURA), Machine learning algorithms for brain tumor segmentation, progression assessment, and overall survival prediction in the brats challenge (BraTS2018), Locating blood vessels in retinal images (STARE), Digital database for screening mammography (DDSM), Automated mining of large-scale lesion annotations and universal lesion detection with deep learning (DeepLesion), Cardiac Magnetic Resonance Images (Cardiac MRI), International skin imaging collaboration (ISIC).

The knowledge of experienced clinical-imagists, follows certain characteristics in images, namely, contrast, color, appearance, topology, shape, edges, etc., It contributes to the performance of medical image interpretation through the use of deep learning models like, anomaly detection models by identifying the characteristics in the image; image segmentation models; image reconstruction models; models for combining two different images into one [15].

The knowledge of imaging doctors can be classified as follows:

- 1. Low-level medical data
  - Areas of attention of physicians in medical images [16].
  - Disease characteristics [17].
- 2. High-level medical data
  - Labels Diagnostic pattern [18],
- 3. Diagnostic training model that represents specific data identified by doctors [19].

The type and volume of medical data, the labels, the category of field knowledge and the methods of their integration into the DL architectures implicitly determine their performance in medical applications [9].

# 2.2. Types of data and datasets

We will further expose, the types of images and medical data used for diagnosis: natural images, medical images, high-level medical data

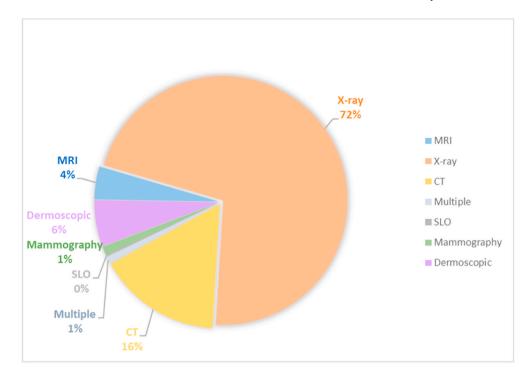


Fig. 1. Imaging and exploratory investigations in the process of image interpretation Acronyms: MRI Magnetic Resonance Images, CT Computed Tomography, SLO Scanning Laser Ophthalmoscopy images, X-ray on weakly-supervised classification and localization of common thorax diseases [9,10].

(diagnostic pattern), low-level medical data (areas of images, disease characteristics), manual features used for medical image analysis.

2.2.1. Natural images – from natural datasets, ImageNet 1 (over 14 million images tagged in 20k categories) and COCO 2 (with over 200 images annotated in 80 categories). Large natural images (ImageNet) are incorporated for the detection of objects in the medical field and are used in applications for the detection of lymph nodes [20], detection of polyp and pulmonary embolism [21], detection of breast tumors [22], detection of colorectal polyps [23,24]. Natural Images, ImageNet, PASCAL VOC "static data" set, Sports-1M video datasets, which is the largest video classification indicator with 1.1 million sports videos in 487 categories [25].

2.2.2. Medical images from external medical datasets of the same diseases in similar ways (e.g., SFM and DM) [26], medical images from external medical datasets of the same diseases in different ways (DBT and MM, ultrasound) [27] or from different diseases [28]. Medical images are used in multiple applications. Multi-modal medical images, PET images are incorporated for the detection of lesions in CT scans of the liver [29]. Multimodal medical images are also used in another model in the detection of liver tumors [30]. Multimodal medical images (mammographic data) are used to detect breast masses [31]. Medical images, (CT, MRI, angio-CT bottom of the eye images), annotated retinal images, used to help segment the heart vessel without annotations [32]. External medical data and images of other diseases, such as the union dataset (3DSeg-8) by aggregating eight sets of 3D medical segmentation data [33].

# 2.2.1. Medical data from doctors: high-level medical data (diagnostic pattern) and low-level medical data (areas of images, disease characteristics)

High-level and low-level medical data: anatomical aspects of the image, shape, position, typology of lesions integrated into segmentation tasks, example of the ISBI 2017 dataset used in skin injury segmentation. The use of additional medical datasets in different ways has also proven to be useful, although most applications are limited in using MRI to help segmentation tasks in CT images [34]. Specific data identified by doctors

(attention maps, hand-highlighted features) increase the diagnostic performance of deep learning networks (no comparative studies have been conducted). Medical data from doctors, handmade features, handcrafted features, invariant LBP, as well as H & Components, are computed first from the images. The use of the BRATS2015 data set in applications in which these features are used is achieved performance in image segmentation by input-level fusion. However, anatomical priorities are only suitable for segmentation of fixed-shaped organs such as the heart or lungs [33].

2.2.4. Manual features used for medical image analysis is a series of measurements (X-ray projections in CT or spatial frequency information in MRI). The methods based on deep learning have been widely applied in this area [35,36]. Examples: image reconstruction with optical diffuse tomography (DOT), reconstruction of magnetic resonance imaging by compressed detection (CS-MRI) [37], reconstruction of the image with diffuse optical tomography (DOT) of limited-angle breast cancer and limited sources in a strong scattering environment [38], recovery of brain MRI images, target contrast using GAN [39]. Content-based image recovery (CBIR) can be great help to for the clinicians to navigate these large data sets. Some deep learning methods adopt transfer learning to use knowledge from natural images or external medical datasets [40–42], for example, metadata such as age and sex of patients, characteristics extracted from health areas, decision values of binary traits and texture traits in the process of thoracic X-ray recovery.

Medical data used to generate medical reports, subtitling medical images, templates from radiologist reports, visual characteristics of medical images, generating reports using the IU-RR dataset.

# 2.3. Addressing label noise in the formation of deep learning patterns in medical image analysis

The noise of the label in the formation of deep learning models is important in their performance for medical image analysis. The approach of the label noise was achieved by: cleaning and preprocessing labels, improving the network architecture with noise layer, the endowment of networks with loss functions, data re-

Imaging	Number of Images	Туре	Purpose	Name Datasets	
Multiple	1921 patients	Brain Breast Prostate Lung	Classification Segmentation	ADNI BACH AGPCH	
MRI	539 patients and 573 controls	Brain	Classification	ABIDE	
MRI	150 patients	Cardiac	Classification	ACDC	
X-ray	112,120 images from 30,805 patients	Chest Detection		Chest X-ray14	
CT X-ray	1018 patients	Lung	Detection	LIDC-IDRI	
СТ	888 images	Lung	Detection	LUNA16	
X-ray	40,895 images from 14,982 patients	Musculo- skeletal	Detection	MURA	
MRI	542 images	Brain	Segmentation	BraTS2018	
SLO	400 images	Eye	Segmentation	STARE	
Mammography	2500 patients	Breast	Classification Detection	DDSM	
СТ	32,735 images from 4427 patients	Multiple	Classification Detection	DeepLesion	
MRI	7980 images from 33 cases	Cardiac	Calssification Segmentation	Cardiac MRI	
Dermoscopic	13,000 images	Skin	Classification Detection Segmentation	ISIC 2018	

Fig. 2. Types of images datasets in the medical domain.

weighting, data and label consistency, training procedures.

### 2.3.1. Cleaning and pre-processing labels

In chest X-ray scans in the classification of thoracic diseases, the smoothing of labels was used to handle noisy labels and led to improvements of up to 0.08 in the area below the characteristic receptor operating curve (ASC) [43].

# 2.3.2. Network architectures

In the case of network architectures, the noise layer proposed by Ref. [44] improved the accuracy in detecting breast lesions in mammograms.

#### 2.3.3. Loss functions

The enhancement of networks with loss functions that cause annotations to dilate with a small and large structuring element to generate noisy masks for the foreground and background, e.g., parts of the ring union image were marked as unsafe regions that were ignored during training [45].

# 2.3.4. Re-weighting data

Re-weighting of data to cope with noisy annotations in cancer detection was achieved by training models on a large group of noisy label patches using calculated features from a small set of clean label patches and increased model performance by 10% [46]. This strategy was used to classify skin lesions in noisy label images [47], for

segmentation of the heart, clavicles and lung in chest X-rays [7], for segmenting the skin lesion from highly inaccurate annotations [48] proposed a specific characteristic of pixels.

# 2.3.5. Consistency of data and labels

For segmentation of the left atrium in the MRI from tagged and unlabelled data it was proposed to form two separate models: a teacher model that produced noisy labels and labelled maps with non-certainties on un-labelled images and a student model that was trained using the noisy labels generated, while taking into account the uncertainty of the label and making correct predictions on the clean data set in accordance with the teacher's model on the label, with uncertainty below the threshold.

# 2.3.6. Training procedures

For segmentation of the bladder, prostate and rectum in MRI, a model was trained on a clean label data set and used it to predict segmentation masks for a separate set of un-labelled data, and a second model was instructed to estimate a confidence map to indicate regions where predicted labels were more likely to be accurate and reliable paper used to sample the main model with a 3% improvement in the Dice similarity coefficient (DSC) [49]. A rather similar method has been used to classify aortic valve defects in MRI [50].

# 2.4. DL model description and classification according to medical data types used, objectives and performances in medical applications

We will synthesize in Fig. 3, Classification of DL models according to the characteristics and tasks for which they were designed, classification of DL models according to the characteristics and tasks for which they were designed [9,10].

DL architectures can be divided into three categories: Supervised DL models:

- Recurrent Neural Network (RNN): Long-short-term memory (LSTM), Gated Recurrent Unit (GRU),
- Convolutive Neural Network (CNN),
- Generative Adversarial Network (GAN).

Unsupervised deep learning models:

- Deep Network of Beliefs (DBN),
- Deep Transfer Network (DTN),
- Tensor Deep Stack Networks (TDSN),
- Autoencoders (AE).

#### 2.4.1. Below we describe the DL models

CNN (convolutive neural network): CNNs are popular in areas where the shape of an object is an important feature, such as image analysis [15,51–54], particularly in the study of cancers and bodily injuries in the medical sector [55,56] and video analysis [57].

We present in the following considerations on training data and learning categories specific to CNN:

- classification data by level of medical information,
- classification-training on medical iterations,
- · hierarchical learning,
- · representative learning,
- · stratified learning optimization of network parameter,
- optimization of network parameters.

The convolutional neural network (CNN) goes through several stages in the classification of medical images, namely, learning to extract non-informative patches and identify non-informative patches through multiple instances.

CNN contains convolutional layers, grouping layers, dropout layers, and an output layer, hierarchically positioned that each learn stun specific characteristics in the image [58].

CNN in image analysis has low performance when high-resolution datasets are considered [59] and when localization over large patches

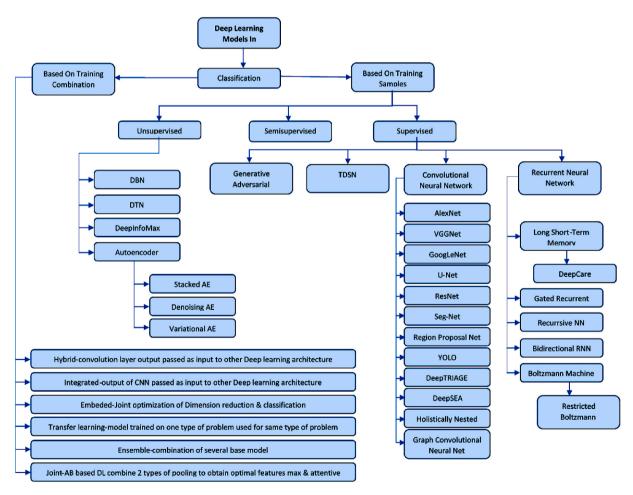


Fig. 3. Classification of DL models according to the characteristics and tasks for which they were designed. Acronyms: Deep Network of Beliefs (DBN), Deep Network of Distribution and Target, Deep Info Max (DIM), AutoEnconder (AE), Generative Adversarial Network (GAN), Tensor Deep Stacking Network (TDSN), Convolutional Neural Network (CNN), Visual Geometry Group Network (VGG Net), Deep Layers Network (GoogLeNet), Fully Convolutional Network (U-Net), Residual Neural Network (ResNet), Deep Segmentation-Emendation Network (SegNet), Region Proposal Net (RPN), You Only Look Once (YOLO), Deep Triage (DT), deep learning—based algorithmic framework (DeepSEA), Holistically-Nested Edge Detection (HED), Graph Convolutional Natural Net (GCNN),Recurent Neuronal Network (RNN), Deep Dynamic Neural Network (Deep Care),Gated Recurrent Network (GRN), Recurrsive RNN(RvNNs), Long Short-Term Memory (LSTM), Bidirectional RNN (BRNN), Restricted Boltzmann Machine (RBM).

is required, especially in medical images [60].

Image analysis performance is enhanced by the use of the following architectures: AlexNet, VGGNet and ResNet, YOLO or U-net that we describe below:

AlexNet was proposed by Refs. [56,57] for the ImageNet Large Scale Visual Recognition Challenge (ILSVRC) in 2012.

AlexNet consists of 8 layers, 5 layers of convolution and 3 dense, fully connected layers, overlapping overlay, abandonment, data augmentation, ReLU activations after each convolutional layer and fully connected, SGD with impulse [56]. AlexNet is used for image recognition in image analysis and is usually applied to issues involving semantic segmentation and high-resolution data classification tasks [61,62].

VGG (Visual Geometry Group): Consists of 13 convolution layers (in VGG16) & 16 convolution layers (in VGG19), 3 dense layers, pooling and three RELU units, very small responsive fields [63]. VGG is used for object recognition, classification of medical images [64,65] and image segmentation [66]. VGG loses accuracy when the depth becomes too high.

ResNet (Residual Neural Network): Contains closed units or closed recurring units and has a strong similarity to recent successful elements applied in RNNs. ResNet is characterized by: residual mapping, identity function; and a two-layer residual block; One layer learns from the residue, the other layer learns from the same function and has high level of performance in image classification (Saravanan et al., Saravanan) and audio analysis tasks [67].

GoogLeNet is built from 22 deep LAYERS CNN and 4 million parameters and contains several layer filters and stacked convolution layers [68]. It was used for batch normalization, image distortions, and RMSprop.

U-Net, developed by Ronneberger [69]. It addresses the problem of locating images of a standard CNN by extracting data features followed by reconstruction of the original dimension through an up-sampling operation. U-Net is a type of Enconder-Decoder network in which the codoficator output belongs to the input space. U-Net is used in single-stage segmentation and classification [70], specifically in the location of cancerous lesions [71–73]. SegNet [74] is a U-Net variant that uses maximum grouping indices in the upsampling step that reduces the complexity of U-Net space.

U-Net-based models:

U-Net [69] and its derivatives segment the medical image with good results. U-Net is based on the FCN structure, consisting of a series of downscaling and upscaling layers and with skip connections between paired convolutional layers in the encoder. U-Net and its variants such as UNet ++ [75] and recurrent U-Net [76] perform well in many medical image segmentation tasks [77–79].

Next, we will present and describe the U-Net-based architectures:

- Attention U-Net Usually for a segmentation task there is only a part
  or a few parts of the image that are relevant for the problem. However, the basic U-Net is not capable of focusing on a specific region of
  interest and that results in excessive processing of irrelevant areas,
- KiU-Net Classical U-Net performs poorly in detecting small structures and does not segment boundaries of regions precisely. This happens because the deeper we go in the

layers of the network, the larger the receptive field is, and this results in a reduced attention to details. A solution to this drawback came with the development of the KiU-Net in 2020 in Ref. [80]. The architecture consists of two networks, a Kite-Net and a U-Net that run in parallel having their results combined, see Fig. 5.

Since Kite-Net alone is only focusing on extracting small structures and the dataset could have both large and small regions to be segmented, it has been put together with U-Net, which performs well at segmenting high-level features, large regions.

• HarDNet - This architecture has been described in Ref. [81] and it has achieved the state-of-the-art on two datasets so far. It appeared as a solution to the failure of U-Net at segmenting small blurry areas, to the lack of coverage for broken image areas and the time-consuming training. It consists of a HarDNet encoder and a partial decoder, which reduces the training time. The encoder is based on a DenseNet but has significantly less connections for cutting computation costs and smaller channel width in order to recover the accuracy lost from connection pruning. The HarDNet block used in encoder is shown in Fig. 6., as an evolution from DenseNet Block. The figure and its description are taken entirely from the original paper [81], see Fig. 6.

U-Net will be enhanced by having a context aggregation block encoder and we will still retain the low-level image features resulting from the U-Net, but we will have slightly finer segmentation of them without adding costs due to context aggregation blocks. Kite-Net will have a unit with attention gates and a Kite-Net decoder, this way we add a benefit of attention to the details of Kite-Net. A partial decoder like the one in the HarDNet-MSEG architecture used as the new U-Net decoder to reduce training time [79].

RNNs were developed by Rumelhart et al. [82] using efficienthly the correlations existing between input data of a prediction problem, through which they process sequential data in relation to text analysis [83–85], in electronic medical records to predict diseases [86,87], and

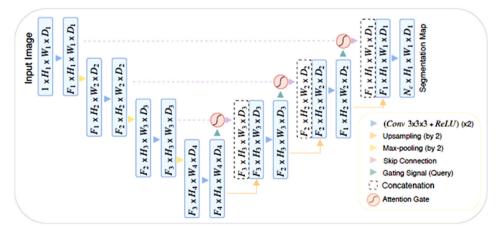


Fig. 4. A block diagram of the proposed Attention U-Net segmentation model. Input image is progressively filtered and down sampled by factor of 2 at each scale in the encoding part of the network (e.g., H4 = H1/8). Nc denotes the number of classes. Attention gates (AGs) filter the features propagated through the skip connections. Feature selectivity in AGs is achieved by use of contextual information (gating) extracted in coarser scales.

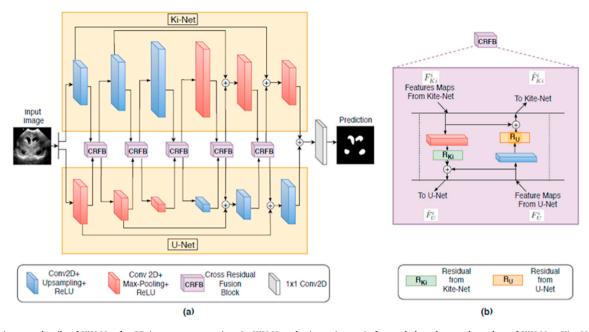


Fig. 5. Architecture details of KiU-Net for 2D image segmentation. In KiU-Net, the input image is forwarded to the two branches of KiU-Net: Kite-Net and U-Net which have CRFB blocks connecting them at each level. The feature maps from the last layer of both the branches are added and passed through 1x1 2D conv to get the prediction. In CRFB, residual features of Kite-Net are learned and added to the features of U-Net to forward the complementary features and vice-versa. (b) Details of Cross Residual Fusion Block (CRFB).

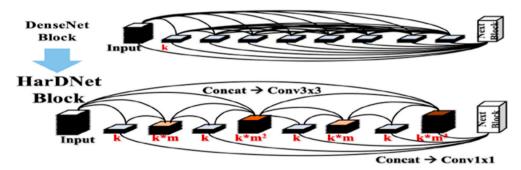


Fig. 6. HarDNet Block overview.

speech recognition [88]. RnN variants are: one-way, learning from the past and predicting the future and bidirectional that uses the future to restore the past. RNN has the following variants: long short-term memory (LSTM) and gated recurring units (GRU), recursive neural networks (Recursive NNs), two-way RNNs (BiRNN). Long-short-term memory LSTMs were introduced by Refs. [65,89] and consist of: the gate of oblivion that alleviates the escape and explosion gradient, the entrance gate and the exit gate, the last two track the flow of data coming in and out of the cell. They were used in speech recognition [90], path prediction [91]and medical diagnosis [92], in which the authors proposed an LSTM network, called DeepCare, combining different types of data to identify clinical diseases.

GRUs (gated recurring unit) created by Refs. [93,94] solve the problem of increasing the time complexity of LSTM, when large amounts of data are used. The GRU consists of a reset gate in which it is decided how much information from the past is transmitted in the future, and an update gate that decides how much information from the past can be forgotten. GRU and LSTMs have similar applications especially in speech recognition [95].

The two-way recurring neural network and the Boltzmann BRNNs introduced by Refs. [96,97] are characterized by the fact that the hidden state is updated by using past information, as in a classic RNN, and by using information related to future moments. They were applied in

handwriting and speech recognition, where they are used to detect missing parts of a sentence in a knowledge of the other words [98,99].

BM models, introduced by Refs. [100,101], are a family of RNNs that are easy to implement and that reproduce many probability distributions, BMs are used in image classification. BMs combined with other models are used to locate object [102,103]. In the classification of images, BMs are used to identify the presence of a tumor [104]. BM models are slow and ineffective when the data size increases exponentially due to the complete connection between neurons [104]. A restricted BM was proposed in which relaxing the connections between neurons of the same or one-way connection between neurons would solve the problem of the classic BM model [105].

AEs, developed by Refs. [82,106], consisting of encoder and decoder, have the aim of reducing the size of the data through significant representations and learning data characteristics for the reconstruction of outputs. They are used in applications in medical image analysis [107], natural language processing [108] and video analysis [109].

Additional variants of AE that can be found in the literature are variational AE (VAE). In a VAE, the encoder is represented by the probability density function of the input into the feature space and, after the encoding stage, a sampling of the new data using the PDF is added. Differently from the DAE and the SAE, a VAE is not a regularized AE, but is part of the generation class.

GAN: It is used to generate synthetic training data from original data using a latent distribution [110]. It consists of two networks, a generator that produces a synthetic data, and a discriminator, which differentiates fake data from real data and separates it in order to increase the quality of the data generated. GAN has two problems: the problem of the collapse of the mode, and the fact that, can become very unstable.

DBN (Deep Network of Beliefs), created by Hinton [111], consists of two networks that build each other: of beliefs represented by an acyclic graph composed of layers of stochastic binary units with weighted and respectively weighted connections, restricted Boltzmann Machines which is a stochastic. DBNs are applied in image recognition and speech recognition, in classification to detect lesions in medical diagnosis and, in video recognition to identify the presence of persons [112], in speech recognition to understand missing words in a sentence [113] and in application on physiological signals to recognize human emotion [114].

DTN contains a characteristic extraction layer, which teaches a shared feature subspace in which marginal source distributions and target samples are drawn close and a layer of discrimination that match conditional distributions by classified transduction [115]. It is used for large-scale problems.

TDSN contains two parallel hidden representations that are combined using a bilinear mapping [116]. This arrangement provides better generalization compared to the architecture of a single module. The prejudices of the generalizers with regard to the learning set shall be inferred. It works effectively and better than an eco-validation strategy when used with multiple generalizers compared to individual generalizers.

Deep InfoMax (DIM): Maximizes mutual information between an input and output of a highly flexible convolutional encoder [117] by forming another neural network that maximizes a lower limit on a divergence between the marginal product of encoder input and output. Estimates obtained by another network can be used to maximize the reciprocal information of the features in the input encoder. The memory requirement of the DIM is lower because it requires only encoder not decoder.

# 2.4.2. Combinations of different DL models depending on the type of data involved in the problem to be solved

DL models can be combined in five different ways depending on the type of data involved in the problem to be solved. Of these, three types of HA (hybrid architectures), namely the integrated model, the built-in model and the whole model [9,10].

In the integrated model, the output of the convolutional layer is transmitted directly as input to other architectures to the residual attention network, the recurrent convolutional neural network (RCNN) and the model of the recurrent residual convolutive neural network (IRRCNN) [118].

In the built-in model (the improved common hybrid CNNBiLSTM), the size reduction model and the classification model perform together, the results of one represent the inputs for the other model. In the model (EJH–CNN–BiLTM), several basic models are combined.

In the transfer learning model (TL) is trained and uses the same type of problem. CNN models that use the TL model are VGG (e.g., VGG16 or VGG19), GoogLeNet (e.g., InceptionV3), Inception Network (Inceptionv4), Recurrent Neural Network (e.g., ResNet50), AlexNet. Joint AB based DL combines max pooling, and careful sharing.

# 2.4.3. Combinations of different DL models to benefit from the characteristics of each model with medical applications are: CNN + RNN, AE + CNN and GAN + CNN

CNN + RNN are used for the capabilities of the CNN feature extraction model and the RNNs [119]. Because the result of a CNN is a 3D value and an RNN works with 2D-data, a remodeling layer is, associated between CNN and RNN, to convert THE production of CNN into an array. CNN + RNN have been successfully applied in text analysis to identify missing words [120] and image analysis to increase the speed of

magnetic resonance image storage [121,122]. CNN + RNN variants are obtained by replacing the Standard RNN component with an LSTM component [22,123].

The AE + CNN architecture combines AE as a pre-training model when using data with high noise levels, and a CNN as a feature extractor model. AE + NVs have an application in image analysis to classify noisy medical images [124] and in the reconstruction of medical images [125, 126].

 ${\rm GAN}+{\rm CNN}$  combines  ${\rm GAN}$  as a pre-workout model to moderate the problem of over-mounting, and a CNN, used as a feature extractor. It has applications in image analysis [8,127].

The DL architectures applied especially in image analysis are CNN, AE and GAN. NVs preserve the spatial structure of the data, and are used as feature extractors (especially U-Net), AEs reduce the characteristics of complex images in the analysis process, and GANs are pre-training architectures that select input categories to control overfitting.

# 3. Applications in medicine and the performance of DL models depending on the therapeutic areas in which they were used

We further highlight the acquisitions in the study of deep learning and its applications in the analysis of the medical image, between 2017 and 2020. You can easily identify references to image labelling and annotation, developing new deep learning models with increased performance, and new approaches to medical image processing:

- diagnosis of cancer by using CNN with different number of layers [128].
- studying deep learning optimization methods and applying in the analysis of medical images [129],
- development of techniques used for endoscopic navigation [130],
- highlighting the importance of data labelling and annotation and knowledge of model performance [131,132],
- perfecting the layer-wise architecture of convolution networks [133], lesson the cost and calculation time for processor training [134],
- description of the use of AI and its applications in the analysis [133] of medical images [135],
- diagnosis in degenerative disorder using deep learning techniques [136]and,
- detection of cancer by processing medical images using the medium change filter technique [137],
- classification of cancer using histopathological images and highlighting the rapidity of Theano, a superior variant of Tensor flow [137],
- development of two-channel computational algorithms using DL (segmentation, extraction of characteristics, selection of characteristics and classification and classification, extraction of high-level captures respectively) [138],
- malaria detection using a deep neural network (MM-ResNet) [5,10].

We will exemplify in Table 1 [139] applications in medicine and the performance of DL models depending on types of medical images and the therapeutic areas in which they were used. We included most relevant papers about the most used medical investigations, respectively medical images.

#### 4. Conclusions

Doctors interpret images descriptively (contour, contrast, appearance, localization, etc.) by using data from different excipients and successive stages in the analysis of medical images. These handcrafted features consume time and do not have a standardized character.

Data quality and volume, annotations and labels, identification and automatic extraction of specific medical terms can help deep learning models perform in the tasks of image analysis. Incorporating these

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Applications and the performances of the DL models depending on the types of medical images and the therapeutic area.

	Type Of Data		Sample		Objective			Model Design	Results	Therapeutic Area	Paper
Mammograph	y Mammography images	Mammography Digital Mammography images and the		f 667 benign and 333 malignant		Detect malign solid lesions and prevent overtreatment in false positives		CNN	AUC of 0.90	Oncology	[103]
	0 1 1					of early maligna gn cysts from ma		Stacked A CNN	ACCURACY OF 0.89 AUC of 0.80	Oncology Oncology	[102] [103]
	Mammography images	15	840 images of mam different patients		Breast arterial calcification evaluate the risk of coron		ms classifier to	CNN	Misclassified cases of 6%	Cardiovascular	[106]
	Digital mammograms		661 from 444 patier	nts	Computer automated esti- density	•	percentage	CNN	AUC of 0.981	Oncology	[140]
	Mammography images Digital mammograms im	Mammography images Digital mammograms images				Segment areas of dense fibro-glandular tissue in the breast Probability of cancer on mammograms		CNN Accuracy of 0.66 CNN AUC of 0.90		Oncology Oncology	[121] [126]
	Type Of Data		Sample		Objective		Model Design	R	esults	Therapeutic Area	Paper
Ultrasound			80 normal echocardiogram images 306 malignant and 136 benign tumors images 3795 vol from the aortic valves from 150 patients		Segment left ventricle in greater precision	system to detect and differentiate t lesions with ultrasound AlexNet, U-Net ResNet Marginal space ling for patients with aortic valve CNNs inspired in AlexNet, U-Net ResNet Marginal space learning			ammoude distance of	Cardiovascular	[141]
	Ultrasound imaging 3				CAD system to detect an breast lesions with ultras					l Oncology	[22]
					•			e deep Position error of 1.66 m and mean corner distance error of 3.29 mms	osition error of 1.66 mms and mean corner istance error of 3.29	s Cardiovascular	[90]
Radiography	Radiography images 42 os Radiographs 11 30 rai		7821 subjects with 6 monitoring phases 420 radiography images (219 control group, 201 osteoarthritis) 112,120 frontal views chest radiographs from 30,805 patients and 17,202 frontal view chest radiographs with a binary class label for normal vs abnormal		CAD for diagnosis of knee osteoarthritis Radiographies CAD for hip osteoarthritis diagnosis Abnormality detection in chest radiographs  CNN  CNN  CNN		Deep Siamese CNN		ccuracy of 0.66 ccuracy of 0.92	Traumatology Traumatology	[120] [142]
							CNN	AUROCs of 0.960 0.951. AUROCs o and 0.893		Radiology	[143]
T	ype Of Data	Sample		Objective		Model Design	Results			Therapeutic Area	Paper
image (l	athology cancer images nematoxylin and eosin) &E colored tissue	Lymphocy	th over 21,000 annotated	Study of tumor tissue samples. Localize areas of necrosis and lymphocyte infiltration Segmentation technique Create a screening system for Malaria		Two CNNs CNNs	AUC of 0.95 Accuracy of 0,9	)2		Oncology Diseases of multiple organs	[144] [145]
sn	iemsa-stained thin blood near slides cell images		ll images 150 infected and			CNN	Accuracy of 0.9	94		Infectious Disease	[86]
	licroscopy image patches		es belonging to 20 categories	Classification of brea microscopy images	st cancer histology	CNN with a Support Vector Machine (SVM)			lass classification and cinoma/non-carcinoma	Oncology	[113]
	licroscopy histopathological nages	breast can		CAD for breast cance diagnosis		CNN	Accuracy of 0.9	0.93		Oncology	[114]
M	licroscope images	200 femal 64	e subjects aged from 22 to	Cervix cancer screen	ing	Multiscale CNN	Mean and stand	lard deviati	on of 0.95 and 0.18	Oncology	[127]
										(continued on n	ext page)

(continued on next page)

Table 1 (continued)

	Type Of Data	Sample	Ot	ojective			Model Design	Results		Therapeutic Area	Pape
	Whole-slide prostate histopathology images	2663 images from 32 who prostate histopathology in		hole-slide hist e malignant re	opathology image	es to outline	CNN	Dice coefficient of 0.72	?	Oncology	[146
	Type Of Data	Sample		Objecti	ve		Model Design	n Results		Therapeutic Area	Pape
Ocular	2D Ocular fundus imag	es 243 retina images		Diagno	se retinal lesions		CNN		curve of 0.86 in	Ophthalmology	[84]
fundus	Ocular fundus images 2	D Over 85,000 images		Diabeti classifie	c retinopathy det	ection and stage	Bayesian CNI	•	s and 0.64 in exudates 99	Ophthalmology	[94]
	Color ocular fundus ima	ages 6679 random sampling ima Diabetic Retinopathy Detec			retinal hemorrha	ges	CNN	AUC of 0.894 a	nd 0.972	Ophthalmology	[101
	Ocular fundus images	168 images with glaucoma		System	to detect and eva	aluate glaucoma	CNN: ResNet U-Net	and AUC of 0.91 an	d 0.84 respectively	Ophthalmology	[14]
	Ocular fundus images	90,000 images with their di	iagnoses		the evolution of athy with fundus		CNN	AUC of 0.95		Ophthalmology	[148
	Fundus images	7000 color fundus images			quality in the con		CNN	Accuracy of 100	0%	Ophthalmology	[149
	AREDS (age related eye disease study) image	2 130,000 fundus images		-	sis of Age-related	l Macular	CNN	94.97 sensitivit	y and 98.32% specificity	Ophthalmology	[138
	Fundus images	219,302 from normal partic hypertension, diabetes mellitus (DM), and any smoking history	cipants without	U	age and sex fron	n retinal fundus	CNN	AUC 0.96		Ophthalmology	[150
		Type Of Data		Sample		Objective		Model Design	Results	Therapeutic Area	Раре
Dermoscop	у	Dermoscopy images		350 imag melanom benign ne	as and 374		AD system for ac elanoma diagnosi		Accuracy of over 0.80	Oncology	[104
		Patient demographics and clinical	images	49,567 ir		Recognize nail lesions	ls nychomycosis	Region-based- CNN	AUC of 0.98, AUC of 0.95, AUC of 0.93, AUC value of 0.82 in the different datasets	Dermatology	[125
		Stress 99mTc-sestamibi or tetrofos perfusion images	min myocardial	1638 pat	ients		oronary disease diction system	CNN	Sensitivity value of 0.82 and 0.69 for both use cases	Cardiovascular	[15]
Arterial lab	oelling	Arterial spin labelling (ASL) perfus	sion images	140 subje	ects	Monitoring ce		CNN	AUC of 0.94	Cardiovascular	[97]
Frames fro	m endoscopy	Frames from endoscopy videos		205 normal and 360 Detection abnormal images of gastroin		Detection and	localization syste inal anomalies vi		CNN AUC of over 0.80	Gastroenterology	[107]
instrume	ataset multi- nt Endo-Visceral and multi-instrument	Single-instrument Retinal Microsus Tracking dataset, Multi-instrument surgery and multi-instrument in vi	Endo-Visceral	frames) a	data (4479 nd 910 or the test data	Detect the two position of dif instruments in and microscop	ferent medical endoscopy	Convolutional Detection regression network	Accuracy of 0.94	Robotic Surgery	[124
	Type Of Data		Sample		Objective			Model Design	Results	Therapeutic Area	Раре
CT/PET- CT/	Nuclear MRIs 3D		124 double ec state from 17	•	Diagnose poss	ible soft tissue in	juries	Deep-Resolve, a 3D- CNN model	MSE of 0.008	Traumatology	[152
SPECT	· ·	ned by Optical Coherence	269 patients v	vith AMD,	Retina age-rela diagnostic	ated macular deg	generation	CNN	AUC of 0	Ophthalmology	[83]
	Tomography 1231-fluoropropyl carbomethoxyiodophenyl nortropane single-photon emission computed tomography (FP-CIT			control patients diagnostic patient cases Automatic interpreta Parkinson's disease							

Table 1 (continued)

	Type Of Data	Sample	Objective		Model Design	Results	Therapeutic Area	Paper
	Abdominal CT 3D images	tomographies	evaluate th	n to classify tomographies and ne malignity degree in gastro- tromal tumors (GISTs)	Hybrid system between convolutional networks and radiomics	AUC of 0.882	Oncology	[153]
	CT image patches 2D	<del>-</del>	CAD systen disease	n to diagnose interstitial lung	CNN	Accuracy of 0.85	Pneumology	[91]
	3D MRI and PET		CAD for early Alzheimer disease stages		Multimodal DBM	Accuracy of 0.95, 0.85 and 0.75 for the three use cases	Neurology- Psychiatry	[99]
	Type Of Data	Sample		Objective	Model Design	Results	Therapeutic Area	Paper
MRI	Diffusion-weighted imaging maps using MRI	222 patients. 187 treated with rtPA (recombinant tissue-type plasminog activator)		Decide Acute Ischemic Stroke patients' treatment through volume lesions prediction	CNN	AUC of 0.88	Neurology- Psychiatry	[53]
	Magnetic resonance images	474 patients with schizophrenia an healthy subjects	nd 607	607 Schizophrenia detection I	Deep discriminant autoencoder network	Accuracy over 0.8	Neurology- Psychiatry	[55]
	Gadoxetic acid-enhanced 2D MRI	144,180 images from 634 patients	Staging liver fibrosis through MR	CNN	AUC values of 0.84, 0.84, and 0.85 for each stage	Neurology- Psychiatry Neurology- Psychiatry	[59]	
	Resting state functional magnetic resonance imaging (rs- fMRI), T1 structural cerebral images and phenotypic information	505 individuals with autism and 52 matched typical controls	spectrum disorders  CAD for early Alzheimer disease stages		Denoising AE		Accuracy of 0.70	[64]
	3D MRI and PET	93 Alzheimer Disease, 204 MCI Mild Cognitive Impairment converters and normal subjects			Multimodal DBM		Accuracy of 0.95, 0.85 and 0.75 for the three use cases	[65]
	Type Of Data	Sample	Objecti	ive	Model Design	Results	Therapeutic Area	Paper
CT/PE' CT/ SPEC	as CT images, MRI images and PET images, and	6776 images for training and 4166 for tests	to the r	y medical diagnostic images accord modality they were produced and illustrations ing to their production attributes	ling CNN and a syner signal system	gic Accuracy of 0.86	Various	[112]
	CT image 2D	63,890 patients with cancer and 171,345 healthy	890 patients with cancer and 171,345 Discriminate		CNN 1	Log-Loss error of 0.6 with a sensitivity of 0.87		[123]
	CT 2D images	3059 images from several parts of human body		up CT images collection and rebuild	I the DenseNet and a deconvolution m	RMSE of 0.00048	Various	[8]
	CT images 3D	6960 lung nodule regions, 3480 of which were positive samples and rest were negative samples (non-nodule)		o diagnose lung cancer in low-dosa ted tomography	ge Eye-tracking spa attentional model and convolutional neural network	rse Accuracy of 0.97	Oncology	[154]
	CT images 2D and text (reports)	9000 training and 1000 testing images	classify	sing text from CT reports in order to their respective images		Accuracy of 0.95, 0. and 0.58 respectivel for the three use case	ly ses	[155]
	Computed tomography (CT)	Three datasets: 224,316, 112,120 and 15,783	Binary classification of posteroanterior characteristics are a second control of the control of		nest CNN	92% accuracy	Radiology	[156]

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	Type Of Data	Sample	Objective	Model Design	Results	Therapeutic Area	Paper
MRI	Clinical characteristics and MRI 3D	135 patients with short-, Medium and long-term survival	Predict the survival of patients with amyotrophic lateral sclerosis	CNN	Accuracy of 0.84	Neurology- Psychiatry	[108]
	Optical coherence tomography images	52,690 AMD patients' images and 48,312 control	Differentiate Age-Related Macular Degeneration lesions in optical coherence tomography	Modification of VGG16 CNN	AUC of 0.92, AUC of 0.93 and AUC of 0.97 for the different use cases	Ophthalmology	[109]
	Lung computed axial tomography 2D images and breast ultrasound lesions	520 breast sonograms from 520 patients (275 benign and 245 malignant lesions) and lung CT image data from 1010 patients (700 malignant and 700 benign nodules)	CAD system to classify breast ultrasound lesions and lung CT nodules	Stacked denoising AE	AUC of 0.94	Oncology	[157]
	MRI 2D	444 images from 195 patients with prostate cancer	CAD to prevent errors in diagnosing prostate	CNN	AUC of 0.94	Oncology	[158]
	MRI 2D	MICCAI 2009 left ventricle segmentation challenge database	Determinate limits between the endocardium and epicardium of the left ventricle	RNN with automatic segmentation techniques	Accuracy of 1.0 in the best case	Cardiovascular	[111]

	Type Of Data	Sample	Objective	Model Design	Results	Therapeutic Area	Paper
MRI	12 categories of medical diagnostic images, such as CT images, MRI images and PET images, and 18 categories of illustrations 12 patients' and 14 patients' CT and MRI images	6776 images for training and 4166 for tests 12 patients' pelvic data and 14 patients' brain data	Classify medical diagnostic images according to the modality they were produced and classify illustrations according to their production attributes Generation of pseudo-CT using MRI imaging for potential treatment with MRI-based radiotherapy planning.	CNN and a synergic signal system CNN	Accuracy of 0.86 Accuracy of 0,98 and 0,95	Various Brain and Pelvic	[112] [159]
	Functional MRI	68 subjects perform 7 activities, and a state of rest	Analyze cerebral cognitive functions	3D CNN, resting state networks	Accuracy of 0.94	Neurology- Psychiatry	[119]
	Liver MRIs	522 liver MRI cases with and without contrast for known or suspected liver cirrhosis or focal liver lesion	Screening system for undiagnosed hepatic magnetic resonance images	CNN	Reduces negative predictive value and leads to greater precision	Gastroenterology	[122]
	MRI images	1064 brain images of autism patients and healthy controls. MRI data from 110 multiple sclerosis patient	Automatically evaluate the quality of multicenter structural brain MRI images	CNN	AUC 0.90 and 0.71	Radiology	[160]

Acronyms: AMD age-related Macular Degeneration, CAD Computer Aided Diagnosis, CNN Convolutional Neural Network, MRI Magnetic Resonance Images, PET Photon Emission Tomography, CT Computed Tomography, OCT Optical Coherence Tomography, D dimensions, AUC Area Under the Curve, MSE Mean Squared Error, RMSE Root Mean Square Error, DSC Dice Similarity Coefficient.

features, labels, into DL architectures increases their performance.

High-level domain knowledge is incorporated as input images, and low-level domain knowledge is learned using specific network structures [33] and, together with direct networking, low-level domain knowledge information can also be used to design training commands when combined with the easy-to-use training model [161].

DL can be a support in solving complex problems of interpretation of medical images and provides the doctor with support in making medical decisions and time for patient care.

Imaging doctors combine data from different stages and experiences as opposed to DL models that incorporate the same types and modes of handcrafted features. Data quality and volume, annotations and labels, identification and automatic extraction of specific medical terms can help deep learning models perform in the tasks of image analysis [9,77].

### 5. Research problems

Problems in medical image analysis can be categorized as follows:

- Identification, automatic extraction and standardization of specific medical terms.
- Representation of medical knowledge,
- Incorporation of medical knowledge.

Problems in medical image analysis are related to:

- Medical images provided as data for deep-street models require: quality, volume, specificity, labelling.
- Providing data from doctors, descriptive data, labels are ambiguous for the same medical and non-standard references
- Laborious time in data processing are problems to solve in the future.
- Lack of clinical trials demonstrating the benefits of using DL medical applications in reducing morbidity and mortality and improving patient quality of life [9,10,162–164].

Luca AR et. all., presents the problems and approaches of using deep learning applications in medicine by highlighting, classifying the emotions, feelings and attitudes of physicians in the practical interaction with AI, providing an aesthetic experience in their color palette (emotions and feelings).

The holistic approach to the doctor-patient-AI relationship is the solution to in-creasing the attention and involvement of doctors in the use of high-performance technologies for support in medical practice. Compliance with performance criteria, ethics, active involvement through knowledge and technology performance in the realization of the medical act can increase the acceptance of doctors in working with AI and implicitly the good results of medical practice with the aim of increasing the quality of life of patients.

#### 6. Future challenges

In traditional machine learning, the common learning process is separated and is carried out only on certain models, data sets and tasks. Therefore, knowledge is not retained or transferred to each other models. Instead, in deep learning, transfer learning can use knowledge such as the weights and characteristics of a pre-trained model to prepare a new model, as well as to address problems in the Roman task that has a smaller amount of data. Transfer learning with deep learning patterns is faster, has improved accuracy and/or needs less training data [9,165].

A new approach to transfer learning, to address the problem of lack of data training in medical imaging tasks is represented by the technique of learning by transfer called dual transfer learning.

We use the learned features to improve the performance of other tasks, such as classification in skin lesions, benign and malignant or in the case of breast lesions classification of breast histological images into four classes: invasive carcinoma, in situ carcinoma, benign tumor and

normal tissue [9,166].

These consist of adapting the domain consisting of transferring data from one domain to another domain by using labels; knowledge graph characterized by the incorporation of multimodal medical data; generating models capable of extracting features unsupervised and easily incorporated into the architecture of DL networks; techniques to search for a particular network architecture according to the defined objectives data [9,10].

The adaptation of the domain consisted of transferring information from a source domain to a target domain, such as adversarial learning [167], and makes it restrict the domain change between source and target domain in input space [168], feature space [169,170], and output space [171,172]. It can be used to transfer knowledge about one set of medical data to another [173], even when they have different modes of imaging or belong to different disease [174,175]. UDA (unsupervised domain adaptation), which uses medical labels, has demonstrated performance in disease diagnosis and organ segmentation [143,173,176, 177].

The knowledge graph has the specifics of incorporating multimodal medical data and achieves performance in medical image analysis and the creation of medical reports [178]. The graphs of medical knowledge describing, the relationship between different types of knowledge, the relationship between different diseases, the relationship between medical datasets and a type of medical data, help deep learning models work [179].

Generativ models, GAN and AE are mainly used for segmentation activities. GAN uses MRI datasets to segment CT images [175,176]. GAN is a type of unsupervised deep learning network used in medical image analysis. AE are used in extracting features, shape priorities in objects such as organs or lesions, completely unsupervised and are easily incorporated into the network formation process [33,180].

Network Architecture Search Technique (NAS) can automatically identify a specific network architecture in computer tasks [181] and promises that utility and performance in the medical field [182].

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# **Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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