# **RESEARCH**

# Medimatrix: innovative pre-training of grayscale images for rheumatoid arthritis diagnosis revolutionises medical image classifcation

Linchen Liu<sup>1</sup>, Yiyang Zhang<sup>2</sup><sup>®</sup> and Le Sun<sup>2\*</sup>

# **Abstract**

Efficient and accurate medical image classification (MIC) methods face two major challenges: (1) high similarity between images of diferent disease classes; and (2) generating large medical image datasets for training deep neural networks is challenging due to privacy restrictions and the need for expert ground truth annotations. In this paper, we introduce a novel deep learning method called pre-training grayscale images with supervised learning for MIC (Medi-Matrix). Instead of pre-training on color ImageNet, our approach uses MediMatrix on grayscale ImageNet. To improve the performance of the network, we introduce ShuffleAttention (SA), a self-attention mechanism. By combining SA with the multiple residual structure (ResSA block) and replacing short-cut connections with dense residual connections between corresponding layers (densepath), our network can dynamically adjust channel attention weights and receive image inputs of diferent sizes, resulting in improved feature representation and better discrimination of similarities between diferent categories. MediMatrix efectively classifes X-ray images of rheumatoid arthritis (RA), enabling efficient screening without the need for expert analysis or invasive testing. Through extensive experiments, we demonstrate the superiority of MediMatrix over state-of-the-art methods and that color is not critical for rich natural image classifcation. Our results highlight the potential of computer-aided diagnosis combined with MediMatrix as a valuable screening tool for early detection and intervention in RA.

**Keywords:** Medical image classifcation, Rheumatoid arthritis, Grayscale images, Pre-training, Computer-aided diagnosis, Deep learning

## **Introduction**

Rheumatoid arthritis (RA) is an autoimmune disease that causes discomfort in small joints and has the potential to afect other limb joints due to immune system dysfunction [[1](#page-10-0)]. However, traditional random forest classifcation methods (e.g., support vector machines [[2\]](#page-10-1) and random forest [\[3](#page-10-2)]) have limitations and limited recent improvements, being time-consuming and inconsistent across objects. Moreover, constructing large medical

imaging datasets from scratch is challenging due to privacy constraints and the need for expert ground truth [\[4](#page-10-3)]. Tschandl et al. [[5](#page-10-4)] presented a large-scale dataset for skin lesion categorization algorithms.

Imaging studies (e.g., X-rays) are essential in the diagnosis of RA and reveal important symptoms of RA (e.g., synovitis, joint space narrowing, joint effusion, and bone stifness) [\[6](#page-10-5)]. Deep neural networks (DNNs), especially convolutional neural networks (CNNs), are widely used in medical image classifcation (MIC) and have shown impressive performance [[7](#page-10-6), [8\]](#page-10-7). Researchers have explored various diagnostic models based on CNNs to diagnose  $RA$  [\[9](#page-10-8)]. These models have shown promising results in detecting bone lesions and erosions and grading symptoms [[10](#page-10-9)].

<sup>\*</sup>Correspondence: lesun1@nuist.edu.cn

<sup>&</sup>lt;sup>2</sup> Department of Jiangsu Collaborative Innovation Center of Atmospheric Environment and Equipment Technology (CICAEET), Nanjing University of Information Science and Technology, Nanjing 210044, China Full list of author information is available at the end of the article

Two common training methods for CNNs are widely used: (1) training a model with randomly initialized weights; and (2) pre-training a model on a similar task and then fne-tuning it on the target task. However, existing deep learning-based diagnostic models often focus on detecting deep lesion features by deepening the network, which may result in the loss of original features [[11\]](#page-10-10).

In recent years, researchers have focused on studying automatic joint space quantifcation for RA diagnosis [[2\]](#page-10-1). Yet, accurately monitoring early-stage joint damage and bone degradation in RA remains challenging due to limited accuracy in prior studies [\[6](#page-10-5)]. Our work addresses this by enhancing algorithm sensitivity and accuracy to the sub-pixel level. This advancement enables rheumatologists to precisely track RA evolution in its early stages annually.

In this paper, we introduce a novel network architecture called *pre-training of grayscale images with supervised learning for MIC (MediMatrix)* for accurate and efficient diagnosis of RA from X-ray images. Inspired by a variant model of U-Net [\[12\]](#page-10-11), since medical images are grayscale, we transform the ImageNet dataset into grayscale images and pre-train them using MediMatrix, followed by fne-tuning with the obtained pre-training weights. The entire procedure is illustrated in Fig. [1](#page-1-0). MediMatrix eliminates the need for repetitive design rules and accurately classifes X-ray images of RA patients into fve categories representing diferent stages of joint erosion and assessing joint damage. This innovative approach improves the diagnosis of RA and facilitates timely and efective treatment. To improve the RA classifcation task, we introduce the *ShuffleAttention (SA)* module and integrate it with a multilayer residual block, known as the *ResSA block*. This combination improves the ability of the network to extract spatial features at diferent scales. In addition, we replace short-cut links with dense residual

Supervise lear<mark>r</mark><br>labeled image Supervised fine-tuning or<br>labeled medical image Supervise learning or<br>labeled RA image ''''''<br>'≏Ne

links, referred to as *densepath*, to address the problem of misalignment between encoder and decoder features. These modifications significantly improve the network's performance in RA classifcation compared to state-ofthe-art approaches. By accurately and efficiently diagnosing RA, MediMatrix can contribute to improved patient care and management. The symbols used in this paper are summarized in Table [1](#page-1-1). The main contributions of this paper are as follows:

- •We present *MediMatrix*, an innovative network for classifying medical images that automates, speeds up, and standardizes the assessment of afected areas in patients with rheumatoid arthritis. This innovative tool has the potential to transform the diagnosis and management of rheumatoid arthritis by enabling more precise and efficient care.
- •To improve our network's multi-scale spatial feature extraction capability, we introduce the SA module. This module is integrated at the end of the convolutional block. Our network can dynamically adjust the channel attention weights of feature maps by combining the SA module with the multiple residual structure (ResSA block) and replacing short-cut connections with dense residual connections between comparable levels (densepath). As a result, our network is able to represent the features better and discriminate similarities more accurately across diferent categories.
- •To pre-train models for natural image classifcation, we used grayscale ImageNet with MediMatrix instead of traditional methods on color ImageNet. Our fndings suggest that color is not necessary for efective natural image classifcation since grayscale models performed comparably to color models on the original ImageNet challenge. Through an extensive experimentation process, we discovered that gray-

<span id="page-1-0"></span>

#### <span id="page-1-1"></span>**Table 1 Defnition of symbols**



scale models, on average, outperformed color models, improving accuracy by  $(1.32 \pm 0.1)\%$ .

#### **Related work**

We present a comprehensive classifcation of RA using both traditional and deep learning methods.

#### **RA image classifcation based on traditional methods**

This section aims to provide a detailed introduction to the application of traditional methods in RA image classifcation, with a focus on risk assessment and early detection.

#### *Assessing the risk of developing RA*

O'Neillet et al. [\[13\]](#page-10-12) proposed a serum proteomic-based regression model to assess arthritis risk. However, this model's limitation is its poor prediction performance for ACPA-positive individuals. Ou et al. [\[6](#page-10-5)] utilized frequency domain phase spectrum to quantify joint space narrowing progression in fnger joint images at baseline and follow-up. But their approach was labor-intensive.

#### *Using holographic data in the diagnosis of RA*

Computer-aided diagnostic methods have shown comparable accuracy to dynamic contrast-enhanced MRI, with the advantage of reduced image analysis time. Nevertheless, there are limited experimental cases using ultrasound images for synovitis classifcation and quantifcation [\[14,](#page-10-13) [15\]](#page-10-14). Alarcon-Paredes et al. [\[16](#page-10-15)] used random forest and wrapper feature selection, but encountered signifcant computational overhead. Aizenberg et al. [[17](#page-10-16)] used atlas-based segmentation and fuzzy C-means clustering, but encountered problems with noisy data and dependence on initial values, limiting generalization across datasets.

#### *Using clinical and sensor data to diagnose RA*

Fukae et al. [[18\]](#page-10-17) implemented an approach that converts clinical data into two-dimensional array images and uses CNN to categorize rheumatoid arthritis (RA) patients. The algorithm produced results that were consistent with the diagnoses of three rheumatology experts. However, the sensitivity of the algorithm was signifcantly afected by the size of the input images. On the other hand, Bardhan et al. [\[19\]](#page-10-18) developed a two-stage classifcation algorithm capable of accurately labeling about three-quarters of knee thermal imager scans. The first stage detects knee joints afected by arthritis, while the second stage identifes knee joints afected by RA.

#### **RA image classifcation based on deep learning**

The application of deep learning methods in assessing the risk of RA has gradually increased.

#### *Using holographic data in the diagnosis of RA*

Chocholova et al. [\[20](#page-10-19)] used glycomic techniques and serum samples to diferentiate healthy individuals, serum-positive RA patients, and serum-negative RA patients. They combined anti-CCP and total RF measurements with RCA carbohydrate analysis based on ELLBA, achieving high accuracy. However, the method's complexity hinders widespread adoption. Heard et al. [\[21](#page-10-20)] utilized artifcial neural network and decision tree methods to classify healthy individuals, RA patients, and OA patients based on a panel of infammatory cytokines from serum samples. However, this method demands extensive training data and computational resources, leading to long training times and overftting susceptibility, and it does not address image noise infuence.

#### *Using clinical and sensor data in the diagnosis of RA*

Fukae et al. [\[18\]](#page-10-17) used AlexNet and ResNet-18 to convert clinical data into two-dimensional array images for arthritis diagnosis. However, this method requires signifcant computational resources and incurs high costs. It is also sensitive to the size of the input image and prone to overftting. Wyns et al. [\[22](#page-10-21)] used the Kochnin neural network (including self-organizing maps) to predict the diagnosis of early arthritis patients. However, the experimental samples did not include indeterminate samples.

#### *Using imaging data to diagnose RA*

Wu and colleagues used DenseNet to classify synovial hyperplasia in ultrasound images to assess RA severity [[15](#page-10-14)]. However, this method is prone to underfitting and overftting, resulting in reduced generalizability, and it requires signifcant memory resources. Hirano et al. [[23](#page-10-22)] used CNN to evaluate imaging fndings of joint destruction in rheumatoid arthritis, but the accuracy of the method is extremely low. Murakami et al. [\[15](#page-10-14)] used the MSGVF snake algorithm and DCNN classifer to identify osteoporosis. They used a triple cross-validation method to validate independent test datasets. However, the training process of this method requires a amount of memory resources.

#### **Discussion**

Comparing with the above methods, MediMatrix has the following advantages: (1) it innovatively employs grayscale images for pre-training, improving the RA

detection accuracy; (2) it includes an innovative attention mechanism, which removes the necessity of specifying the size of the input image and helps the network extract features in multi-scale space; and (3) it utilizes short-circuit linking to dynamically regulate the attention weights of the channels of the feature maps, thus improving feature representation.

#### **MediMatrix**

#### **Overall network architecture**

The MediMatrix network architecture (Fig. [2](#page-3-0)) is built based on inspiration from a variant of U-Net [\[12](#page-10-11)] to enhance its performance. The network can be divided into three main parts: pre-training, the feature encoding and decoding part.

During the pre-training phase, we use the proposed MediMatrix in an innovative way to train the grayscale ImageNet. Then, we utilize the weights obtained from the pre-training to initialize the same model for labeled RA images. Lastly, we fne-tune the obtained weights using our proposed model.

In the coding part, we replace the convolution block in the traditional U-net with an improved Multi-ResNet block, called ResSA block, proposed in "[ResSA block"](#page-3-1) section. This modification helps to capture more comprehensive and informative features.

In the decoding section, an innovative approach called [Densepath](#page-4-0) is introduced in "Densepath" section. The purpose of this technique is to overcome the semantic gap that exists between the encoder and decoder features. Unlike the traditional U-Net architecture, which uses

a direct connection between the encoder and decoder, Densepath allows for an improved flow of information, resulting in more accurate reconstructions. This method enhances the network's ability to generate accurate representations of the input data, resulting in improved diagnostic accuracy for arthritis damage detection using X-ray images.

Given that the task involves medical image classifcation, we include a softmax layer at the end of the decoding part to generate prediction probabilities for the input image across fve categories. All convolutional blocks in the network utilize the Rectifed Linear Unit (ReLU) activation function and are normalized.

#### <span id="page-3-1"></span>**ResSA block**

The ResSA block (Fig.  $3$ ), represents a sophisticated approach to image feature extraction. This advanced block uses three sets of 3×3 convolutional blocks, each with dense connections for optimal efficiency. In addition, to better incorporate spatial information into the model, a 1×1 convolutional block is used for the residual

<span id="page-3-2"></span>

<span id="page-3-0"></span>



<span id="page-4-1"></span>

**Channel Attention Modu** pooling Feature **Input features** Conv layer Sigmoid **Snatial attenti Spatial Attention Modul-Fig. 6** The process of feature processing in SA

<span id="page-4-2"></span>connection. By summing the outputs of both the dense and the residual connections, the resulting output of the ResSA block (denoted *O* here) emerges as a powerful representation of the original image.

To enhance the convolution layer's ability to select and integrate multi-channel subfeatures, we introduced the SA module (Fig. [4](#page-4-1)). This module divides the combined output *O* of the convolutional layer into multiple sets of subfeatures. Each subfeature is individually processed using spatial and interchannel attention mechanisms, resulting in processed subfeatures. The processed subfeatures are then merged via the channel shuffle operation to fuse the features. This approach enhances the model's selective emphasis on the most relevant information and facilitates the integration of diverse features, thereby improving performance.

#### <span id="page-4-0"></span>**Densepath**

The Densepath (Fig.  $5$ ), addresses the problem of incompatible feature fusion in the U-Net decoding process. The traditional U-Net architecture uses shortcut connections between corresponding layers, which can cause low-level feature information to propagate to the high-level decoding network, leading to feature fusion incompatibility.

<span id="page-4-3"></span>To solve this problem, we propose to replace the shortcut connection with a dense residual connection. This approach ensures a more balanced propagation of feature information throughout the network and improves feature fusion compatibility. By incorporating the dense residual connection, the densepath bridges the semantic gap between encoder and decoder features, enabling accurate feature reconstruction.

#### **ShuffleAttention**

SA (Alg. 1) is an efficient attention mechanism module based on the partial structure of the Convolutional Block Attention Module (CBAM) [[24](#page-10-23)], which combines spatial and channel information, in contrast to Senet, which focuses only on the channel. The feature processing is shown in Fig. [6](#page-4-3).

The channel attention module works in the following steps: First, the input feature map undergoes global max pooling and global average pooling separately based on its width and height. Next, the resulting outputs are fed into a fully connected layer. The element-wise multiplication of this Multi-Layer

Perceptron (MLP) output and the input feature map generates the necessary input features for the Spatial Attention. These steps form the channel attention mechanism.

The channel attention module performs spatial dimension compression on the feature map by obtaining a onedimensional vector and applying operations to it. This compression includes both average pooling and maximum pooling to aggregate spatial information from the feature map. The aggregated information is then passed through a shared network to compress the spatial dimensions of the input feature map. The resulting compressed feature map is summed and fused element-wise to produce a channel attention map. Channel attention focuses on the importance of each element in the feature map. Mean pooling provides feedback for every pixel point in the feature map, while max pooling provides feedback for gradients only at locations where the response is highest in the feature map during gradient back-propagation calculations (Eq. [1\)](#page-5-0).

$$
M_{c}(F) = \sigma(MLP(AvgPool(F)) + MLP(MaxPool(F)))
$$
  
=  $\sigma\left(W_{1}\left(W_{0}\left(F_{avg}^{c}\right)\right) + W_{1}\left(W_{0}\left(F_{max}^{c}\right)\right)\right)$  (1)

where  $\sigma$  is a sigmoid operation,  $MLP$  is a multilayer perceptron, *F* stands for feature.  $F_{avg}^c$  and  $F_{max}^c$  are the average and maximum pooling in the channel attention module.

The *MaxPool* operation extracts the maximum value across the channel for each spatial location, resulting in a feature map with the same height and width. The *AvgPool* operation calculates the average value across the channel for each spatial location, resulting in a feature map with the same height and width. These two extracted feature maps, each with a single channel, are then combined to obtain a new feature map (Eq. [2](#page-5-1)).

$$
\mathbf{M}_{\mathbf{s}}(\mathbf{F}) = \sigma \left( f^{7 \times 7}([\text{AvgPool}(\mathbf{F}); \text{MaxPool}(\mathbf{F})]) \right)
$$
  
=  $\sigma \left( f^{7 \times 7} \left( \left[ \mathbf{F}_{\text{avg}}^{\text{s}}; \mathbf{F}_{\text{max}}^{\text{s}} \right] \right) \right)$  (2)

where  $F_{avg}^s$  and  $F_{max}^s$  are the average pooling and maximum pooling in the spatial attention module. 7×7 indicates the size of the convolution kernel, a 7×7 convolution kernel works better than a 3×3 convolution kernel.

# Algorithm 1: ShuffleAttention **Input:** input\_tensor: input tensor **Output:** Output tensor with attention 1 function ChannelAttention(inputs) 1.  $avg\_pool \leftarrow GlobalAveragePooling2D(inputs)$ 2. max\_pool  $\leftarrow$  GlobalMaxPooling2D(inputs) 3. fc1  $\leftarrow$  Dense(units = num\_filters/8.  $activation = ReLU)(avg-pool)$ 4. fc2  $\leftarrow$  Dense(units = num\_filters,  $\text{activation} = \text{ReLU}(\text{fc1})$ 5. channel\_attention  $\leftarrow$  Multiply([fc2, inputs]) return channel\_attention function SpatialAttention(inputs) 1. conv $1 \leftarrow \text{Conv2D}(\text{filters} = 1,$  $\text{kernel\_size} = (3, 3), \text{padding} = \text{same})(\text{inputs})$ 2. sigmoid  $\leftarrow$  Activation(sigmoid)(conv1) 3. spatial\_attention  $\leftarrow$  Multiply([sigmoid, inputs]) return spatial\_attention function ShuffleAttention(inputs) 1. channel\_attention  $\leftarrow$  ChannelAttention(inputs) 2. spatial\_attention  $\leftarrow$  SpatialAttention(channel\_attention) return spatial\_attention

#### <span id="page-5-0"></span>**Loss function**

<span id="page-5-1"></span>MediMatrix uses the Eq.  $(3)$  $(3)$  as loss function. This function quantifes the dissimilarity between two probability distributions: the actual probability distribution and the predicted probability distribution of the same random variable. By evaluating the cross-entropy loss, the model can assess how well it approximates the target classes by comparing the predicted probabilities to the actual probabilities. A lower value of the cross-entropy loss indicates a higher model performance in terms of accurately predicting the target classes.

<span id="page-5-2"></span>Loss = 
$$
-\frac{1}{N} \sum_{i=1}^{N} \sum_{k=1}^{K} I(y_i = k) \log (p_k)
$$
 (3)

$$
I(x) = \begin{cases} x = 1 & \text{True} \\ x = 0 & \text{False} \end{cases}
$$
 (4)

where *N* is the total number of samples, *K* is the number of categories, *I* is the indicator function, and  $p_k$  represents the probability that the category is *k*

#### **Experiment**

### **Datasets**

The article presents representative images of each cat-egory in the knee osteoarthritis dataset (Fig. [7](#page-6-0)). The dataset comprises a total of 9786 samples. For assessing the severity of osteoarthritis in the knee radiographs, the Kellgren–Lawrence (K–L) classifcation, a qualitative assessment method, was employed. Specially trained medical raters graded the arthritis severity on the radiographs, providing labeled training data for MediMatrix. The different disease stages represented by the grading are outlined in Table [2.](#page-6-1)

For data partitioning, we divide the data set into a training set (70%), a validation set (20%), and a test set (10%). This division allows us to train and optimize Medi-Matrix on the training set, tune the hyperparameters using the validation set, and evaluate the model's performance on the unseen test set. To ensure equal sensitivity to each category, the number of images for each category is consistent across all datasets.

We used the Knee X-ray Images dataset  $[25]$  $[25]$  for scalability experiments (Table  $3$ ). The dataset contains DICOM-standard images with dimensions of 1345  $\times$ 2455. The images were collected based on demographic features, including age, gender, blood type, occupation, and weight. Among the 532 patients, there were 301 females and 231 males.

<span id="page-6-0"></span>

#### <span id="page-6-2"></span>**Table 3 KL grades assigned by 2 Medical Experts**



#### **Experiment settings and metrics**

In our experimental evaluation of the multi-label classifcation of knee joint severity, we used the following evaluation indicators:  $\mu F1$ , balanced accuracy, AUC, and Cohen's Kappa score.

Micro *F*1 ( $\mu$ *F*1): The *F*1 score is the harmonic mean of Precision and Recall.  $\mu F1$  is the average of the *F*1 scores calculated for all categories, regardless of class imbalance. We utilize the *F*1 score to assess the overall multilabel classifcation capability of the model.

Balanced Accuracy (BA): Balanced accuracy is the average accuracy calculated for all categories, taking into account the sample imbalance between diferent categories. It is obtained by assigning weights to the accuracy of each category.

Area Under the Curve (AUC): AUC is the area under the receiver operating characteristic (ROC) curve. The ROC curve represents the relationship between the true positive rate (recall rate) and the false positive rate. AUC measures the performance of the classifer at diferent thresholds and is an efective measure of accuracy.

Cohen's Kappa Score: Cohen's Kappa is a statistical index used to measure the consistency between the classifer and the random selection. It takes into account the correctness of the classifcation and the infuence of random selection. MediMatrix is a multi-class imbalance problem, and Cohen 's Kappa can well evaluate the multiclass classifcation ability.

Using these metrics, we can evaluate the performance

<span id="page-6-1"></span>



<span id="page-7-0"></span>**Table 4 Results of grayscale and color images on SimCLR**

Architecture	Color		Grayscale		
	Top-1 (%)	Top-5 (%)	Top-1	Top-5	
ResNet-50 $(1x)$	68.33	88.02	67.92	87.64	
$ResNet-50(2x)$	73.24	91.40	7291	90.92	
$ResNet-50(4x)$	76.35	93.12	7598	92.85	

joint severity. In addition, given the similarity in severity between grades 1, 2 and 3, we also calculated the AUC (one-to-one) between grades 1 and 2 and between grades 2 and 3 to specifcally measure the classifcation performance in discriminating between these pairs.

Our model is built in a pytorch box  $\mu$  frame. All samples are standardized to facilitate subsequent computation and storage. The epoch in the model is set to 100, the AdamW with a learning rate of 1e-3 is updated, and the experiment runs on an NVIDIA GeForce GTX 3090 GPU and an Intel Core i7-12700 H CPU.

#### **Pretraining protocol**

This study investigated the effectiveness of pre-training using MediMatrix. No signifcant diference was observed in the classifcation performance of grayscale and color images. Additionally, this was demonstrated using SimCLR  $[26]$  $[26]$ —ResNet-50 (1×), ResNet-50 (2×), and ResNet-50  $(4x)$  [\[27](#page-10-26)]. Complying with the approach proposed by SimCLR [[26\]](#page-10-25), two fully connected layers were used to transform the ResNet outputs into 128-dimensional embeddings (Table [4\)](#page-7-0).

To assess the performance of ImageNet models, we measured Top-1 and Top-5 accuracy for various architectures. Our aim was to compare the efectiveness of color and grayscale images, demonstrating that color is not the primary criterion for ImageNet image classification. Surprisingly, the model trained and evaluated on grayscale ImageNet performed just  $(0.4 \pm 0.07)$ % worse than

#### <span id="page-7-2"></span>**Table 6 Experimental performance after fne-tuning**



the color model. Moreover, our results emphasize that pre-training on ImageNet complements pre-training on unlabeled medical images, highlighting its importance in improving performance. We further validated our fndings by experimenting with other state-of-the-art (SOTA) methods (Table [5\)](#page-7-1).

#### **Fine-tuning protocol**

During the fne-tuning process, we initialize the weights of the pre-trained network with the aim of utilizing them for the downstream task.

To optimize the performance of each combination of pretraining approach and downstream fne-tuning task, we conduct a comprehensive hyperparameter search. This involves performing a grid search across seven logarithmically spaced learning rates, ranging from  $10^{-3.5}$ to  $10^{-0.5}$ , as well as three logarithmically spread weight decay values, ranging from  $10^{-5}$  to  $10^{-3}$ . Through this search process, we determine the optimal learning rate and weight decay for each specifc case.

We apply the same search approach when training from the supervised training baseline. Remarkably, we fnd that regardless of the fne-tuning settings, achieving optimal performance typically requires 100 epochs of training. In addition, based on extensive experiments, our grayscale model outperforms the color model in improving the disease recognition rate (Table [6](#page-7-2)). Our grayscale model improves the average accuracy of disease by about  $(1.32 \pm 0.1)\%$ .

#### <span id="page-7-1"></span>**Table 5 Classifcation results on grayscale and color images on top of ImageNet**



#### **Comparative experiments**

In order to assess the efectiveness of our preprocessed dataset, we conducted ample comparative experiments with fve diferent methods on the preprocessed dataset: MobileNetv2 [ $33$ ], CNN + Ordered Loss [ $34$ ], the Extrusion-Excitation Block (SE Block) [\[35](#page-11-2)], DeepKnee [\[36](#page-11-3)], and Set [[37](#page-11-4)].

Designed specifcally for image classifcation and object detection tasks on devices with limited computing resources, MobileNetv2 uses lightweight design and deep separable convolution with linear bottleneck structures to reduce computation and model size. CNN + Ordinal Loss addresses overftting in image classifcation by incorporating ordinal loss, a loss function used to handle ordered categories, into the CNN classifcation model to improve its performance. The Squeeze-Excitation Block (SE Block) [\[38](#page-11-5)] is a mechanism that improves the representational ability of convolutional neural networks by adaptively adjusting the importance of each channel in the feature map. It includes a squeeze phase and an excitation phase, learning the relationship between feature channels to improve the model's representational ability. DeepKnee is a neural network specifcally designed for automatic analysis and diagnosis of knee X-ray images, using convolutional neural networks to extract features, classify and predict joint disease. Finally, Ensemble, which combines the prediction results of multiple basic models, enhances classifcation performance by using models of diferent architectures or initialized with diferent training data and parameters, leading to improved accuracy in the prediction.

Quantitative results: The quantitative results (Table [7](#page-8-0)) of our comparative experiments demonstrate the superiority of MediMatrix over the fve evaluated methods in terms of  $\mu F1$ , balance accuracy, and Cohen's Kappa score. MediMatrix achieved the best performance in these evaluation metrics, indicating its efectiveness in accurately classifying the degree of arthritis damage.

In terms of  $\mu F1$ , MediMatrix outperformed all other methods, achieving the highest average *F*1 score across all categories. This indicates that our model has a strong multi-label classifcation ability and can efectively capture the nuances of diferent knee joint severity levels.

Furthermore, MediMatrix exhibits the highest balance accuracy, efectively considering the sample imbalance among different categories. This achievement demonstrates our model's superior ability to achieve balanced and accurate classifcation performance across all severity levels, even in the presence of variations in sample distribution.

A signifcant achievement is that the AUC results of MediMatrix are comparable to those of the SE block. Our model demonstrated competitive performance in distinguishing between specifc severity levels (e.g., grade 1 and 2) with AUC being a widely used metric to measure classifier performance under different thresholds. These results indicate MediMatrix's efectiveness in discriminating intermediate severity levels, which are often challenging to classify accurately.

Furthermore, our method achieved the highest Cohen's Kappa value of 0.6846 among all methods. Cohen's Kappa measures the agreement between classifer predictions and pre-annotated scores, taking into account the efect of random selection. The high Cohen's Kappa value indicates a strong agreement between our model's predictions and the ground truth scores assigned by medical raters, implying a higher level of reliability and accuracy in our classifcation results.

Overall, these quantitative results demonstrate the superior performance of MediMatrix compared to the evaluated methods, underscoring its efficacy in accurately classifying knee joint severity and predicting consistency with pre-annotated scores. The visualized data for comparison with the results of some SOTA methods are shown in Fig. [8.](#page-9-0) As shown in it, our proposed model has an overall advantage over other SOTA methods.

#### **Ablation experimentnt**

In our ablation experiments, we examined the efectiveness of two key components in MediMatrix: the attention mechanism (SA) and the respath module. To evaluate the attention mechanism, we removed the SA module from the convolution block in the base

<span id="page-8-0"></span>**Table 7 Comparison of results with some SOTA methods (Bold: The best, Italics: The second best)**

Method	$\mu$ F1	BA	<b>AUC</b>	Kappa	AUC(1,2)	AUC(2,3)		
MobileNetV2	0.5104	0.3532	0.7822	0.2554	0.6208	0.6191		
$CNN + Ordinal loss$	0.6865	0.6638	0.8950	0.5557	0.7298	0.8576		
SE block	0.7336	0.7237	0.9237	0.6237	0.7866	0.9265		
DeepKnee	0.3956	0.5078	0.7456	0.2287	0.5931	0.7398		
Ensemble	0.7405	0.7342	0.7342	0.6327	0.7896	0.9360		
MediMatrix	0.7941	0.8059	0.9136	0.6846	0.8948	0.8865		



<span id="page-9-0"></span>MultiResUNet architecture. The network architecture for this attention ablation experiment consisted of the MultiRes block, Respath, and Softmax layers. The results showed a decrease in network accuracy and Cohen's Kappa value (0.5257), indicating the critical role of the SA module in improving spatial feature extraction at different scales. The attention mechanism in MediMatrix enhances the extraction and integration of multi-scale features, resulting in improved classifcation performance.

Next, we investigated the efectiveness of the Respath module, which compensates for spatial information loss during encoder-to-decoder propagation. In this ablation experiment, we replaced the respath module with a direct link. The network architecture for this Respath ablation experiment included the ResSA block, normal path (without Respath), and Softmax layers (Fig. [9](#page-9-1)).

The inclusion of the Respath module allowed the network to retain more spatial information during encoderto-decoder propagation. As a result, the accuracy of the network showed a signifcant improvement over the Respath-enabled configuration. The specific performance metrics are shown in Fig. [9](#page-9-1). These results highlight the importance of the Respath module in preserving spatial information and its impact on improving the overall accuracy of MediMatrix.

In summary, the ablation experiments confrmed the efectiveness of the attention mechanism and the Respath module in MediMatrix. The ShuffleAttention module



<span id="page-9-1"></span>improved multiscale spatial feature extraction, resulting in improved accuracy and Cohen's Kappa Score. The respath module compensated for spatial information loss and significantly improved network accuracy. These modules played a critical role in achieving the superior performance of MediMatrix, as demonstrated by the results.

#### **Generalizability experiments**

To assess the generalizability of the MediMatrix classifcation framework, we performed generality proof experiments using the Knee X-ray Images dataset  $[25]$  $[25]$ . This dataset consists of X-ray images, similar to our original dataset, and contains five categories. The dataset was divided into training, test and validation sets in a ratio of 7:2:1. The results of MediMatrix on the training, validation, and test sets are 91.45%, 89.23% and 88.72%.

#### **Case study**

MediMatrix holds great promise for future RA treatment and integration into intelligent healthcare facilities. This method can improve the diagnostic accuracy and decision-making capabilities of medical professionals who can use it to optimise the treatment of RA patients. It can streamline diagnosis, reduce the time required to make an accurate diagnosis, and initiate timely treatment. By using a data-driven approach to RA diagnosis, MediMatrix holds the promise of improving patient outcomes. In addition, by seamlessly integrating with electronic health records, patient monitoring systems, and telemedicine platforms, MediMatrix has the potential to facilitate interdisciplinary collaboration among healthcare

professionals. It can also contribute to a more holistic approach to healthcare.

#### **Conclusion**

The paper introduces MediMatrix, a novel network that uses pre-trained grayscale images for assessing thermographic images in patients with RA in a fast and automated manner. Shuffle attention has been added to MediMatrix to improve multiscale spatial feature extraction by replacing shortcut connections with dense residual connections, which reduces parallax. The experimental results demonstrate that MediMatrix is superior to the existing methods and has achieved higher diagnostic accuracy on the RA X-ray dataset. Through the use of deep learning and attention mechanisms, MediMatrix provides a cost-efective diagnostic approach and a reliable automated solution for RA diagnosis. This benefits healthcare professionals and patients through improved medical decision-making and care. In the future, we will examine how self-supervised learning can enhance MediMatrix by addressing the problem of inadequately labeling medical images.

#### **Data availability**

The labeled datasets used to support the fndings of this study are available from the corresponding author upon request.

#### **Declarations**

#### **Conflict of interest**

We affirm that we have no commercial or associative interests that could create a confict of interest related to the submitted work.

#### **Author details**

<sup>1</sup> Department of Rheumatology, Zhongda Hospital, School of Medicine, Southeast University, Nanjing 210009, China. <sup>2</sup> Department of Jiangsu Collaborative Innovation Center of Atmospheric Environment and Equipment Technology (CICAEET), Nanjing University of Information Science and Technology, Nanjing 210044, China.

#### Received: 31 July 2023 Accepted: 8 September 2023 Published: 26 September 2023

#### **References**

- <span id="page-10-0"></span>1. Goebel A, et al. The autoimmune aetiology of unexplained chronic pain. Autoimmun Rev. 2022;21:103015.
- <span id="page-10-1"></span>2. Nakatsu K, Morita K, Yagi N, Kobashi S. Finger joint detection method in hand x-ray radiograph images using statistical shape model and support vector machine, 2020, pp. 1–5. IEEE.
- <span id="page-10-2"></span>3. Ainsworth RI, et al. Systems-biology analysis of rheumatoid arthritis fbroblast-like synoviocytes implicates cell line-specifc transcription factor function. Nat Commun. 2022;13:6221.
- <span id="page-10-3"></span>4. Xie Y, Richmond D. Pre-training on grayscale imagenet improves medical image classifcation; 2018.
- <span id="page-10-4"></span>5. Tschandl P, Rosendahl C, Kittler H. The ham10000 dataset, a large collection of multi-source dermatoscopic images of common pigmented skin lesions. Sci Data. 2018;5:1–9.
- <span id="page-10-5"></span>6. Ou Y, et al. A sub-pixel accurate quantifcation of joint space narrowing progression in rheumatoid arthritis. IEEE J Biomed Health Inform. 2022;27:53–64.
- <span id="page-10-6"></span>7. Zhou Q, Huang Z, Ding M, Zhang X. Medical image classifcation using light-weight CNN with spiking cortical model based attention module. IEEE J Biomed Health Inform. 2023;27:1991–2002.
- <span id="page-10-7"></span>8. Qu Z, Sun H. A secure information transmission protocol for healthcare cyber based on quantum image expansion and grover search algorithm. IEEE Trans Netw Sci Eng. 2022.
- <span id="page-10-8"></span>9. Mate GS, Kureshi AK, Singh BK. An efficient CNN for hand x-ray classification of rheumatoid arthritis. J Healthc Eng. 2021.
- <span id="page-10-9"></span>10. Rohrbach J, Reinhard T, Sick B, Dürr O. Bone erosion scoring for rheumatoid arthritis with deep convolutional neural networks. Comput Electr Eng. 2019;78:472–81.
- <span id="page-10-10"></span>11. Tan W, et al. Segmentation of lung airways based on deep learning methods. IET Image Proc. 2022;16:1444–56.
- <span id="page-10-11"></span>12. Ibtehaz N, Rahman MS. Multiresunet: rethinking the u-net architecture for multimodal biomedical image segmentation. Neural Netw. 2020;121:74–87.
- <span id="page-10-12"></span>13. O'Neil LJ, et al. Proteomic approaches to defining remission and the risk of relapse in rheumatoid arthritis. Front Immunol. 2021;12:729681.
- <span id="page-10-13"></span>14. Hu X, et al. Joint landmark and structure learning for automatic evaluation of developmental dysplasia of the hip. IEEE J Biomed Health Inform. 2021;26:345–58.
- <span id="page-10-14"></span>15. Wu M, et al. A deep learning classifcation of metacarpophalangeal joints synovial proliferation in rheumatoid arthritis by ultrasound images. J Clin Ultrasound. 2022;50:296–301.
- <span id="page-10-15"></span>16. Alarcón-Paredes A, et al. Computer-aided diagnosis based on hand thermal, RGB images, and grip force using artifcial intelligence as screening tool for rheumatoid arthritis in women. Med Biol Eng Comput. 2021;59:287–300.
- <span id="page-10-16"></span>17. Aizenberg E, et al. Automatic quantifcation of bone marrow edema on MRI of the wrist in patients with early arthritis: a feasibility study. Magn Reson Med. 2018;79:1127–34.
- <span id="page-10-17"></span>18. Fukae J, et al. Convolutional neural network for classifcation of twodimensional array images generated from clinical information may support diagnosis of rheumatoid arthritis. Sci Rep. 2020;10:1–7.
- <span id="page-10-18"></span>19. Bardhan S, Bhowmik MK. 2-stage classifcation of knee joint thermograms for rheumatoid arthritis prediction in subclinical infammation. Australasian Phys Eng Sci Med. 2019;42:259–77.
- <span id="page-10-19"></span>20. Chocholova E, et al. Glycomics meets artifcial intelligence-potential of glycan analysis for identifcation of seropositive and seronegative rheumatoid arthritis patients revealed. Clin Chim Acta. 2018;481:49–55.
- <span id="page-10-20"></span>21. Heard BJ, et al. A computational method to differentiate normal individuals, osteoarthritis and rheumatoid arthritis patients using serum biomarkers. J R Soc Interface. 2014;11:20140428.
- <span id="page-10-21"></span>22. Wyns B, et al. Prediction of diagnosis in patients with early arthritis using a combined Kohonen mapping and instance-based evaluation criterion. Artif Intell Med. 2004;31:45–55.
- <span id="page-10-22"></span>23. Hirano T, et al. Development and validation of a deep-learning model for scoring of radiographic fnger joint destruction in rheumatoid arthritis. Rheumatol Adv Pract. 2019;3:rkz047.
- <span id="page-10-23"></span>24. Woo S, Park J, Lee, J-Y, Kweon IS. Cbam: convolutional block attention module, 2018; pp. 3–19.
- <span id="page-10-24"></span>25. Gornale S, Patravali P. Digital knee x-ray images. Mendeley Data 2020;**1**.
- <span id="page-10-25"></span>26. Chen T, Kornblith S, Norouzi M, Hinton G. A simple framework for contrastive learning of visual representations, pp. 1597–1607 (PMLR, 2020).
- <span id="page-10-26"></span>27. He K, Zhang X, Ren S, Sun J. Deep residual learning for image recognition, 2016; pp. 770–778.
- <span id="page-10-27"></span>28. He K, Fan H, Wu Y, Xie S, Girshick, R. Momentum contrast for unsupervised visual representation learning, 2020; pp. 9729–9738.
- <span id="page-10-28"></span>29. Cao Z, Yu H, Yang H. Sano A. Pirl: participant-invariant representation learning for healthcare using maximum mean discrepancy and triplet loss. arXiv preprint [arXiv:2302.09126](http://arxiv.org/abs/2302.09126) 2023.
- <span id="page-10-29"></span>30. Henaff O. Data-efficient image recognition with contrastive predictive coding, pp. 4182–4192 (PMLR, 2020).
- <span id="page-10-30"></span>31. Tian Y, Krishnan D, Isola P. Contrastive multiview coding. New York: Springer; 2020. p. 776–94.
- <span id="page-10-31"></span>32. Donahue J, Simonyan K. Large scale adversarial representation learning. Adv Neural Inf Process Syst 2019;**32**.
- <span id="page-11-0"></span>33. Sandler M, Howard A, Zhu M, Zhmoginov A, Chen LC. Mobilenetv2: inverted residuals and linear bottlenecks. In: Proceedings of the IEEE conference on computer vision and pattern recognition 2018.
- <span id="page-11-1"></span>34. Chen P, Gao L, Shi X, Allen K, Yang L. Fully automatic knee osteoarthritis severity grading using deep neural networks with a novel ordinal loss. Comput Med Imaging Graph. 2019;75:84–92.
- <span id="page-11-2"></span>35. Jie et al. Squeeze-and-excitation networks. IEEE Trans Pattern Anal Machine Intell 2019.
- <span id="page-11-3"></span>36. Tiulpin A, Thevenot J, Rahtu E, Lehenkari P., Saarakkala, S. Automatic knee osteoarthritis diagnosis from plain radiographs: a deep learning-based approach; 2017.
- <span id="page-11-4"></span>37. Tiulpin A, Saarakkala S. Automatic grading of individual knee osteoarthritis features in plain radiographs using deep convolutional neural networks. Diagnostics. 2020;10:932.

<span id="page-11-5"></span>38. Hu J, Shen L, Sun G. Squeeze-and-excitation networks, 2018; pp. 7132–7141.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.