Attention-Guided Discriminative Region Localization for Bone Age Assessment

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Abstract. Bone age assessment (BAA) is clinically important as it can be used to diagnose endocrine and metabolic disorders during child development. Existing deep learning based methods for classifying bone age generally use the global image as input, or exploit local information by annotating extra bounding boxes or key points. Training with the global image underutilizes discriminative local information, while providing extra annotations is expensive and subjective. In this paper, we propose an attention-guided approach to automatically localize the discriminative regions for BAA without any extra annotations. Specifically, we first train a classification model to learn the attention heat maps of the discriminative regions, finding the hand region, the most discriminative region (the carpal bones), and the next most discriminative region (the metacarpal bones). We then crop these informative local regions from the original image and aggregate different regions for bone age regression. Extensive comparison experiments are conducted on the RSNA pediatric bone age data set. Using no training annotations, our method achieves competitive results compared with existing state-of-the-art semi-automatic deep learning-based methods that require manual annotation. Codes are available at https://github.com/chenchao666/Bone-Age-Assessment.

Keywords: Bone Age Assessment · Hand Radiograph · Attention Map · Discriminative Region Localization.

1 Introduction

Bone age assessment (BAA) from hand radiograph images is a common technique for investigating endocrinology and growth disorders [15], or for determining the final adult height of children [1]. In clinical practice, BAA is usually performed by examining the ossification patterns in a radiograph of the non-dominant hand, and then comparing the estimated bone age with the chronological age. A discrepancy between the two values indicates abnormalities [17]. The most widely used manual BAA methods are Greulich-Pyle (GP) [8] and Tanner-Whitehouse (TW) [1]. In the GP method, bone age is estimated by comparing the whole hand radiograph with a reference atlas of representative ages, while the TW method examines 20 specific regions of interest (ROIs) and assigns scores based
Fig. 1. Illustration of sample images from RSNA and the learned attention heatmaps of discriminative regions. (a) Four sample images from the RSNA dataset. (b) Original image with attention-guided localization of three discriminative regions. (c) The learned attention map of the hand region (H). (d) The learned attention map of the most discriminative region, which is denoted as Region-1 (R1). (e) The learned attention map of the next most discriminative region, which is denoted as Region-2 (R2).

on a detailed local structural analysis. The TW method is more reliable, but time consuming, while the GP method is relatively quick and easy to use. In both manual solutions, reliable and accurate bone age estimation is limited by the subjective influence of a trained radiologist.

Over the past decades, numerous automated image analysis methods and tools have been developed for BAA. These methods can be divided into two groups: non-deep learning based methods [5, 6, 14, 18] and deep learning based methods [4, 10–12, 17]. Early representative non-deep learning-based methods mainly extract hand-designed features from the whole images or specific ROIs, and then train a classifier with no more than 2,000 samples. The performance of these methods is quite limited, with results ranging from 10-28 months mean absolute difference (MAD) [17]. Deep CNNs [7, 13] and a large scale BAA data set introduced by the Radiological Society of North America (RSNA) [10] have enabled recent advances to achieve impressive performance, with some exceeding an expert’s performance [9, 11]. Specifically, BoNet [17] designed an ad-hoc CNN for BAA, the author exploited the deformation layer to address bone non-rigid deformation, and achieved a result of 9.5 months MAD on average. In [11], in order to crop specific local regions, the author first trained an U-Net model to segment the hand region with 100 labeled hand masks and then trained a key point detection model to achieve image registration. As a result, they achieved a 6.30 months MAD for males and 6.49 months MAD for females. The winners of the RSNA challenge [3] achieved a 5.99 months MAD with their best model and achieved a 4.26 months MAD by averaging 50 predictions (utilizing 5 top models with 10 augmented images). In the current best performing method, [4] presented a new framework based on a local analysis of anatomical ROIs, the author provided extra bounding boxes and key point annotations during training, and performed hand detection and hand pose estimation to exploit local information for BAA. As a result, they achieved the best result in RSNA, 4.14 months MAD.
Fig. 2. Our approach consists of two stages. In the first stage, we train a classification model to learn the attention maps for the hand region, the most discriminative region, and the next most discriminative region. Guided by these heat maps, we crop the ROIs from the original image. In the second stage, we train a regression model to perform age regression by aggregating different ROIs.

In this work, we mainly concentrate on deep learning approaches for BAA. The difficulties of using deep learning for BAA are: (1) Raw input images are quite large (about 2000 × 1500 pixels), but ossification patterns are usually hidden in specific small ROIs. Therefore, downsizing the raw images into low-resolution images will lose important information, decreasing the final performance. (2) Raw images can be poorly aligned. As shown in Fig. 1(a), the ROIs can be very small with undetermined position, which also reduces model performance. While recent work has proposed to localize ROIs [4] or use image alignment [11], these methods rely on providing extra masks, bounding boxes, or keypoint annotations. To address these limitations, we present a novel attention guided deep learning-based framework for BAA. As shown in Fig. 1, our method uses attention to automatically identify the hand region, the carpal bones, and the metacarpal bones. By leveraging the local information in these ROIs, our approach achieves competitive results without requiring manual annotations.

2 Methodology

As shown in Fig. 2, our proposal consists of two phases: a localization phase and an age regression phase. In the localization phase, we train a classification model to learn the attention heatmaps for the hand region, the most discriminative region, and the next most discriminative region. Guided by these attention maps,
we crop the local regions from the original image. In the regression phase, we
train a regression model to aggregate different ROIs for bone age regression.

2.1 Phase I: Attention Guided ROIs Localization

Weakly supervised detection and localization methods that aim to identify the
location of the object in a scene only using image-level labels have been widely
used for many tasks [9, 16, 19, 20]. Inspired by these methods, we propose to
utilize learned heat maps to identify the discriminative local patches for BAA.
As shown in Fig. 2(a), for a given CNN model and an input image, let \( F \in R^{H \times W \times C} \) denotes the activation outputs of the last convolutional layer. The
resulting feature maps are then fed into a global average pooling (GAP) or
global max pooling (GMP) layer [20], followed by a fully connected (FC) layer.
For convenience, we only consider the case of using the GAP layer and ignore
the bias term. We denote the average value of the \( k \)-th feature map as \( S_k = \frac{1}{H \times W} \sum_{i,j} F_{ijk} \), \( k = 0, 1, \ldots, C - 1 \), and denote the weight matrix of the FC layer as \( W \in R^{C \times T} \), where \( T \) is the number of classes in the classification model. In this
way, the value of the \( t \)-th output node can be calculated as

\[
\hat{Y}_t = \sum_{k=0}^{C-1} W_{kt} S_k = \frac{1}{H \times W} \sum_{i,j} \sum_{k=0}^{C-1} W_{kt} F_{ijk}
\]

(1)

where \( \hat{Y} \in R^T \) is the network output and \( W_{kt} \) denotes the connection weights
between the \( k \)-th input nodes and \( t \)-th output nodes in the last FC layer. Therefore, for the \( t \)-th class samples, we define a heat map \( A_t \in R^{H \times W} \) as,

\[
A_t(i, j) = \sum_{k=0}^{C-1} W_{kt} F_{ijk}
\]

(2)

The final output of \( t \)-th node, therefore, can be calculated as

\[
\hat{Y}_t = \frac{1}{H \times W} \sum_{i,j} A_t(i, j)
\]

(3)

In this respect, for a given image that is assigned to class \( t \), the heat map \( A_t \)
indicates the contribution of each pixel to the final classification result. After
obtaining the heat map \( A_t \), we resize the it to the original image size and design
a binary mask \( M_t \) to identify the most discriminative regions of a given image.

\[
M_t(i, j) = \begin{cases} 
1 & A_t(i, j) \geq \tau \\
0 & A_t(i, j) < \tau 
\end{cases}
\]

(4)

where \( \tau \) is a threshold that determines the size of the ROIs, A larger \( \tau \) leads
to a smaller ROI, and vice versa. We empirically set \( \tau = 40 \) throughout the
experiments. Guided by the binary mask, we can crop the high-resolution discrimi-
native local patches from the original images.
Implementation Details For the classification model, we adopt the InceptionV3 (without top layers) as the backbone network for feature extraction, and then add a GMP (or GAP) layer followed by a FC layer with 240 output nodes, which is the maximum age of the children in the data set in months. When we utilize the original one-hot labels for training, the network fails to converge. We believe the reason is that hand images with different ages are similar, but have different one-hot labels. Hence, we utilize soft labels for training. For a hand image and its labeled age $t$, we define the following function to soften the label distribution

$$Y_i = \begin{cases} 1 - \frac{|i - t|}{\delta} & |i - t| \leq \delta \\ 0 & |i - t| > \delta \end{cases}$$  

(5)

where $Y \in R^T$ is the ground-truth label distribution and $i = 0, 1, \ldots, 239$. $\delta$ controls the smoothness of the label distribution, a larger $\delta$ leads to a smoother label distribution. In the experiments, we set $\delta = 50$. We utilize the weights pre-trained in ImageNet, and train the network with the Adam optimizer with a batch size of 32. The network is trained over 70 epochs, the learning rate is set to 0.0003 for the first 50 epochs and set to 0.0001 for the last 20 epochs.

Localization of Region-1 To localize the most discriminative region (Region-1), we train the classification model with the original images which have been resized to $560 \times 560$. The activation outputs $F \in R^{18 \times 18 \times 2048}$ are then fed into a GMP layer which follow by the last FC layer. The localization of the Region-1 can therefore, be given by the binary mask in Eq. 4.

Localization of Region-2 To localize the next most discriminative region (Region-2), we generate input images by replacing the pixels in Region-1 with random values. As shown in Fig. 3(f), training the classification network using the images with Region-1 "erased" forces the network to make predictions based on the pixels other than those in Region-1. In this way, we can localize Region-2 in the same way as localizing Region-1.

Localization of Hand Region The introduced method tends to localize a small discriminative task-relevant region [19]. To make the attention heat maps focus on the whole hand region, we utilize a smaller input image by resizing the original images to $300 \times 300$. In this way, each pixel in the feature map $F \in R^{8 \times 8 \times 2048}$ will correspond to a larger image patch in the original image. We also use the GAP layer instead of the GMP layer, which further helps concentrate on a larger discriminative region.

2.2 Phase II: Bone Age Regression

As shown in Fig. 2(b), the second phase aggregates local regions by feeding them into different input channels. We adopt the Xception [2] without top layers as the backbone network, followed by a convolutional layer, a max pooling layer, and a FC layer. To effectively utilize gender information, we concatenate the image features with the gender features, which takes gender information (1 for male and -1 for female) as input and feeds it through a FC layer with 32 neurons. The
concatenated features are then fed into the last FC layer. The network is trained with the Adam optimizer by minimizing the mean absolute error (MAE):

\[
\text{loss} = \frac{1}{n} \sum_{i=1}^{n} |\hat{y}_i - y_i|
\]

(6)

where \(n\) is the number of training samples, \(\hat{y}_i\) is the output of the regression model, and \(y \in \{1, 2, \cdots, 240\}\) is the ground-truth age. The weights of the backbone network are initialized with weights pre-trained on ImageNet, and we train the network with the Adam optimizer using a batch size of 16. The whole network is then trained for 120 epochs. The learning rate is set to 0.0003, 0.0001, and 0.00001 for the first 60 epochs, the next 30 epochs, and the final 30 epochs, respectively.
3 Experiments

Dataset and Evaluation Protocol We evaluate the performance of our approach using the RSNA dataset \[10\], which contains 14,036 clinical radiographs. The example hand images can be seen in Fig. 3(a). All the hand images are in arbitrary size (about 2000 × 1500) and each image contains bone age (1-240) and gender information (0 and 1 for male and female). During the experiments, we randomly split the dataset into three splits, with 500 samples each for validation, and testing, and the other images are used for training. We take the mean absolute error (MAE) as the loss function and evaluation criteria throughout the experiments.

Visualization As shown in Fig. 3, to demonstrate the effectiveness of the attention-guided discriminative region localization, we show six representative images and their corresponding attention maps and cropped images. Fig. 3 reveals several interesting observations: (1) Although the hand region in the original images are in various angles and arbitrarily-sized, the learned attention maps can always localize the hand region accurately. (2) The carpal bones are identified as the most informative and discriminative local regions, which is consistent with the manually determined ROIs in the TW-based method \[17\]. (3) The joints of the metacarpal bones are recognized as the next most discriminative regions, which is also consistent with ROIs marked by radiologists \[11\]. (4) Compared to the original images, the hand region, Region-1, and Region-2 are much better aligned across different hand images.

Performance of baseline networks We train four common CNN networks without gender information to perform bone age regression with the input image size set to 224 × 224. Table 1 shows that Xception \[2\] achieves the best performance, and initializing the model by the weights pre-trained from ImageNet performs much better than training from scratch. We also investigate the influence of the gender information and image size. As observed in Table 2: (1) Utilizing gender information improves performance with Xception backbone. (2) Increasing the input image size improves performance, but does not help when the image size is larger than 560 × 560. Therefore, in the following experiments, we set the input image size to 560 × 560.

| Network       | Vgg19 | InceptionV3 | ResNet50 | Xception |
|---------------|-------|-------------|----------|----------|
| w/o & w pre-train | 12.2  | 9.3         | 10.9     | 9.2      | 11.3     | 9.3   | 9.9   | 8.8   |

Aggregating Local Regions for BAA To evaluate the effectiveness of our proposal, we perform BAA by utilizing a single local region or aggregating different local regions for bone age regression. The performance comparison between our proposal and four state-of-the-art deep learning methods \[3, 4, 11, 17\] are shown in Table 3. We observe that: (1) Existing state-of-the-art methods have
Table 2. Experimental results with different image sizes using gender information (Xception as backbone)

| Image size   | 224×224 | 336×336 | 448×448 | 560×560 | 720×720 |
|--------------|---------|---------|---------|---------|---------|
| MAE          | 7.8     | 7.6     | 7.4     | 7.3     | 7.3     |

Table 3. Comparison between our proposal and state-of-the-art methods.

| Methods | Image Size | Extra Labels | Data Augment | Model Ensembling | MAE  |
|---------|------------|--------------|--------------|------------------|------|
| [11]    | 750×750    | mask & keypoint | Yes          | 18 model results | 6.4  |
| [17]    | 224×224    | No            | Yes          | No               | 9.5  |
| [3]     | 512×512    | No            | Yes          | No               | 5.99 |
| [4]     | 500×500    | Bbox & keypoint | Yes          | No               | 4.14 |
| Ours    | O          | H            | R1          | R2               | H+R1 | R1+R2 | O+H+R1 | H+R1+E | H+R1+R2 |
| MAE     | 7.3        | 6.3          | 6.1         | 7.0              | 5.4  | 5.6   | 5.4    | 4.7    | 4.8    |

achieved promising results, but these methods rely on extra annotations, such as hand masks, bounding boxes (denoted as Bbox), and keypoints to train a segmentation or detection network [4, 11], or rely on averaging multiple model results to get better performance [3, 11]. (2) Our method can achieve good results only with the Hand region (H) or Region-1 (R1). (3) Performing BAA based on any local region achieves better performance than utilizing the Original image (O), which shows the advantages of using the local high-resolution patches for BAA. (4) Aggregating different local regions further improves the final results, with the best results of 4.8 and 4.7 achieved by fusing the "H+R1+R2" or "H+R1+E" ("E" denotes the original image with Region-1 "erased"). Our method does not use any extra annotations, data augmentation, or ensemble strategies, while achieving a performance that is competitive with techniques requiring additional supervision.

4 Conclusion

In order to improve the performance of BAA, existing methods have attempted to exploit local information by providing extra annotations and training segmentation or detection networks. In this work, we introduce an attention guided method to localize the discriminative local regions with only image-level labels, which is more practical and objective. In particular, we can accurately localize hand region, carpal bones (Region-1), and joints of the metacarpal bones (Region-2). By aggregating different local regions for BAA, we achieve a competitive result on the RSNA bone age data set. In future work, we will integrate the local region localization phase and age regression phase into a unified end-to-end learning framework.
References

1. Helen Carty. Assessment of skeletal maturity and prediction of adult height (tw3 method), 2002.
2. François Chollet. Xception: Deep learning with depthwise separable convolutions. In *Proceedings of the IEEE conference on computer vision and pattern recognition*, pages 1251–1258, 2017.
3. Bilbily A. Cicero, M. Machine learning and the future of radiology: how we won the 2017 rsna ml challenge. 2017.
4. María Escobar, Cristina González, Felipe Torres, Laura Daza, Gustavo Triana, and Pablo Arbeláez. Hand pose estimation for pediatric bone age assessment. In *International Conference on Medical Image Computing and Computer-Assisted Intervention*, pages 531–539. Springer, 2019.
5. Arkadiusz Gertych, Aifeng Zhang, James Sayre, Sylwia Pospiech-Kurkowska, and HK Huang. Bone age assessment of children using a digital hand atlas. *Computerized medical imaging and graphics*, 31(4-5):322–331, 2007.
6. Daniela Giordano, Concezio Spampinato, Giacomo Scariciofalo, and Rosalia Leonardi. An automatic system for skeletal bone age measurement by robust processing of carpal and epiphysial/metaphysial bones. *IEEE Transactions on Instrumentation and Measurement*, 59(10):2539–2553, 2010.
7. Ian Goodfellow, Yoshua Bengio, and Aaron Courville. *Deep learning*. MIT press, 2016.
8. Pyle S.I. Greulich, W.W. Radiographic atlas of skeletal development of the hand and wrist, 1959.
9. Qingji Guan, Yaping Huang, Zhun Zhong, Zheyong Zheng, Liang Zheng, and Yi Yang. Diagnose like a radiologist: Attention guided convolutional neural network for thorax disease classification. *arXiv preprint arXiv:1801.09927*, 2018.
10. Safwan S Halabi, Luciano M Prevedello, Jayashree Kalpathy-Cramer, Artem B Mamonov, Alexander Bilbily, Mark Cicero, Ian Pan, Lucas Araújo Pereira, Rafael Teixeira Sousa, Nitamar Abdala, et al. The rsna pediatric bone age machine learning challenge. *Radiology*, 290(2):498–503, 2019.
11. Vladimir I Iglovikov, Alexander Rakhlin, Alexandr A Kalinin, and Alexey A Shvets. Paediatric bone age assessment using deep convolutional neural networks. In *Deep Learning in Medical Image Analysis and Multimodal Learning for Clinical Decision Support*, pages 300–308. Springer, 2018.
12. Hyunkwang Lee, Shahein Tajmir, Jenny Lee, Maurice Zissen, Bethel Ayele Yeshiwas, Tarik K Alkasab, Garry Choy, and Synho Do. Fully automated deep learning system for bone age assessment. *Journal of digital imaging*, 30(4):427–441, 2017.
13. Geert Litjens, Thijs Kooi, Babak Ehteshami Bejnordi, Arnaud Arindra Adiyoso Setio, Francesco Ciompi, Mohsen Ghafoorian, Jeroen Avm Van Der Laak, Bram Van Ginneken, and Clara I Sánchez. A survey on deep learning in medical image analysis. *Medical image analysis*, 42:60–88, 2017.
14. Ewa Pietka, Sylwia Pospiech-Kurkowska, Arkadiusz Gertych, and Fei Cao. Integration of computer assisted bone age assessment with clinical pacs. *Computerized medical imaging and graphics*, 27(2-3):217–228, 2003.
15. Andrew K Poznanski, Ramiro J Hernandez, Kenneth E Guire, Ulana L Bereza, and Stanley M Garn. Carpal length in children: useful measurement in the diagnosis of rheumatoid arthritis and some congenital malformation syndromes. *Radiology*, 129(3):661–668, 1978.
16. Ramprasaath R Selvaraju, Michael Cogswell, Abhishek Das, Ramakrishna Vedantam, Devi Parikh, and Dhruv Batra. Grad-cam: Visual explanations from deep networks via gradient-based localization. In Proceedings of the IEEE international conference on computer vision, pages 618–626, 2017.

17. Concetto Spampinato, Simone Palazzo, Daniela Giordano, Marco Aldinucci, and Rosalia Leonardi. Deep learning for automated skeletal bone age assessment in x-ray images. Medical image analysis, 36:41–51, 2017.

18. Hans Henrik Thodberg, Sven Kreiborg, Anders Juul, and Karen Damgaard Pedersen. The bonexpert method for automated determination of skeletal maturity. IEEE transactions on medical imaging, 28(1):52–66, 2008.

19. Xiaolin Zhang, Yunchao Wei, Jiashi Feng, Yi Yang, and Thomas S Huang. Adversarial complementary learning for weakly supervised object localization. In Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, pages 1325–1334, 2018.

20. Bolei Zhou, Aditya Khosla, Agata Lapedriza, Aude Oliva, and Antonio Torralba. Learning deep features for discriminative localization. In Proceedings of the IEEE conference on computer vision and pattern recognition, pages 2921–2929, 2016.