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KCB-Net: A 3D knee cartilage and bone segmentation network via sparse annotation

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Abstract

Knee cartilage and bone segmentation is critical for physicians to analyze and diagnose articular damage and knee osteoarthritis (OA). Deep learning (DL) methods for medical image segmentation have largely outperformed traditional methods, but they often need large amounts of annotated data for model training, which is very costly and time-consuming for medical experts, especially on 3D images. In this paper, we report a new knee cartilage and bone segmentation framework, KCB-Net, for 3D MR images based on sparse annotation. KCB-Net selects a small subset of slices from 3D images for annotation, and seeks to bridge the performance gap between sparse annotation and full annotation. Specifically, it first identifies a subset of the most effective and representative slices with an unsupervised scheme; it then trains an ensemble model using the annotated slices; next, it self-trains the model using 3D images containing pseudo-labels generated by the ensemble method and improved by a bi-directional hierarchical earth mover's distance (bi-HEMD) algorithm; finally, it fine-tunes the segmentation results using the primal-dual Internal Point Method (IPM). Experiments on four 3D MR knee joint datasets (the SKI10 dataset, OAI ZIB dataset, Iowa dataset, and iMorphics dataset) show that our new framework outperforms state-of-the-art methods on full annotation, and yields high quality results for small annotation ratios even as low as 10%.

Keywords

Knee cartilage and bone segmentation; Sparse annotation; Ensemble learning; 3D MR images

1. Introduction

Osteoarthritis (OA) is a prevalent chronic disease caused by the damage and degeneration of cartilages. It is estimated that 20% of Americans may suffer from various levels of OA by 2030. Magnetic resonance imaging (MRI) has become a common technique for studying and

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Declaration of competing interest

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assessing changes within the knee joint, including cartilages and bones. Fig. 1 illustrates the anatomical structure of the knee joint.

Considering the knee joint anatomy, the femoral cartilage (FC), tibial cartilage (TC), patellar cartilage (PC), and menisci (M) are the main tissues affecting the knee joint health. To quantitatively measure the thickness of the knee cartilages and identify the bone–cartilage interface, accurate cartilage and bone segmentation is needed.

To capture the detailed structure of the knee anatomy, 3D MR images are commonly scanned at high in-plane resolution. However, labeling 3D MR images is very timeconsuming.

In this paper, we propose a new framework, KCB-Net, for segmenting knee cartilages and bones in 3D MR images with sparse annotation. We first encode each 2D slice in an unlabeled training set of 3D images into a feature vector in an unsupervised manner. Second, a subset of the most representative slices (based on a given annotation ratio) for the training set is selected for experts to label. Third, we train three 2D modules using the selected labeled slices. Fourth, preliminary pseudo-labels of the training set are generated by the trained 2D modules, which are further used to train a 3D module. Fifth, we ensemble the three 2D modules and one 3D module, and generate pseud-labels of the entire training set, which are used to re-train the four modules and the 3D ensemble model for a few iterations. The feature maps generated by the ensemble model are post-processed to produce the final segmentation results.

We conduct experiments on four 3D MR knee joint datasets (the SKI10 dataset, OAI ZIB dataset, Iowa dataset, and iMorphics dataset; see Section 4). Our experiments show that with full annotation, our new KCB-Net framework outperforms state-of-the-art full annotation methods, and with sparse annotations, KCB-Net yields high quality results even with very sparse annotation ratios (e.g., 10%).

2. Related work

Automated and semi-automated methods for knee joint segmentation have been investigated for several decades. Shape models, graph optimization approaches, and deep learning (DL) methods exhibited high performance in recent years. 3D graph based methods are well suited for knee cartilage segmentation. Yin et al. (2010) proposed a layered optimal graph image segmentation for multiple objects and surfaces (LOGISMOS) framework to simultaneously segment multiple interacting surfaces of objects by incorporating multiple spatial interrelationships of surfaces in a D-dimensional graph. Kashyap et al. (2017) extended the LOGISMOS framework to simultaneously segment 3D knee objects for multiple follow-up visits of the same patient — effectively performing optimal 4D (3D + time) segmentation. Xie et al. (2022) proposed a primal–dual Internal Point Method (IPM) to first learn the parameters of the surface cost functions for the LOGISMOS algorithm and then solve an optimization problem for the final segmentation.

Several deep convolutional neural network (CNN) approaches showed close-to-human level performance. Liu et al. (2018) proposed a fully automatic musculoskeletal tissue

segmentation method that integrates CNN and 3D simplex deformable approaches to improve the accuracy and efficiency. Ambellan et al. (2019) combined the strengths of statistical shape models and CNN to successfully segment knee bones/cartilages. Tan et al. (2019) proposed a method to first extract the regions of interest (ROIs) for three cartilage areas and then fuse the three ROIs to generate fine-grained segmentation results. Couteaux et al. (2019) presented an approach to localize and segment knee menisci and classify MRI slices based on tears in anterior and posterior menisci and their orientations using Mask R-CNN (He et al., 2017).

Zheng et al. (2019) proposed a 3D segmentation method that ensembles three 2D models and one 3D model (called base-learners). It first trains the base-learners using labeled data, and ensembles the base-learners by training a meta-learner (Yu et al., 2017). It then re-trains the base-learners and meta-learner with pseudo-labels to obtain a 3D segmentation model. However, such base-learners still rely on fully annotated 3D data. Zheng et al. (2020b) further proposed a sparse annotation strategy to select the most representative 2D slices for annotation. It first encodes each slice into a low-dimensional vector, and prioritizes the slices based on their representativeness in a set of 3D images. Next, three 2D modules and one 3D module (a 3D FCN (Çiçek et al., 2016) are trained, and pseudo-labels of the unlabeled data are generated using the base-learners. A Y-shape DenseVoxNet (Yu et al., 2017) is used to train a meta-learner, which ensembles the 2D and 3D modules. Zheng et al. (2020a) then extended this sparse annotation strategy, and designed a K-head FCN to compute the pseudo-label uncertainty of each slice and rule out highly uncertain pixels in the subsequent training process.

3. Method

3.1. Overview

Our KCB-Net combines and extends previously reported ensemble learning (Zheng et al., 2019) and sparse annotation (Zheng et al., 2020b) methods for 3D segmentation. Fig. 2 shows its main steps.

(1) Representative slice selection: As in Zheng et al. (2020b), each 2D slice in every major orientation red(i.e., *axial, coronal*, or *sagittal*) in the entire set W of 3D training images is encoded as a low-dimensional latent vector, and all slices are prioritized by their representativeness. The top-ranked k slices are selected as the ones, in which to perform expert annotations.

(2) Base-learner training and pseudo-label generation: As in Zheng et al. (2019), three 2D modules, one for each *axial, sagittal*, or *coronal* orientations, are trained on the selected and annotated slices. Once 2D modules are trained, pseudo-labels are assigned to all remaining un-annotated slices in W and a 3D module is trained. K-UNet mechanism (Chen et al., 2016) is newly used to extract multi-scale features. Each module extracts information across different scales to support fine-scale feature extraction. Instead of using sparse 3D FCN (Çiçek et al., 2016) as in Zheng et al. (2020b), we utilize 3D Attention UNet (Oktay

et al., 2018), which uses labels of the expert-annotated slices and pseudo-labels of all the un-annotated slices.

As in Guo et al. (2021), an edge-aware branch is added to the 3D module to increase the weights of cartilage and bone surface locations. To explore the appearance consistency among consecutive slices and further improve the quality of the pseudo-labels generated, the H-EMD method (Liang et al., 2022) is newly enhanced by incorporating a bi-directional hierarchical earth mover's distance (bi-HEMD) when generating pseudo-labels of the un-annotated slices. Our bi-HEMD method first produces object candidates by applying multiple threshold values on the probability maps, and then selects object instances by minimizing the earth mover's distance based on a reference set of the object instances.

(3) Ensembling and self-training : Following the pseudo-label generation, 2D and 3D modules are ensembled by training a 3D Y-shape DenseVoxNet (Zheng et al., 2019) as a meta-learner using the original input images and pseudo-labels, which learns the target object segmentation from the labels/pseudo-labels. The output of the ensemble model is utilized to iteratively re-train the modules in Step (2) and the ensemble model in Step (3), repeated until convergence.

(4) Post-processing : We newly add a post-processing step exploiting the task-specific characteristics that knee bones and cartilages are anatomically adjacent with one other. A fine-tuning network (Xie et al., 2022) that incorporates the surface interrelationships between adjacent bones and cartilages is trained by taking the probability maps generated in Step (3) as input and the pseudo-labels as the learning targets. The fine-tuning network is optimized using the IPM algorithm (Xie et al., 2022).

3.2. Representative slice selection

Identifying a small-enough set of the most representative 2D slices for annotation that subsequently facilitates the segmentation method training is critical for the success of our proposed approach. This section presents our slice selection scheme, called representative annotation (RA).

Medical experts often annotate a 3D image by choosing one orthogonal plane (axial, coronal, or sagittal) and labeling the corresponding slices one by one. It may, however, be beneficial to annotate 2D slices along each of the three orthogonal planes. Fig. 3 illustrates the slice selection method.

3.2.1. Slice representation—For a specified annotation ratio (e.g., 10% of all slices), to select the most representative slices to label, we first need to efficiently represent the slices. Medical image slices can commonly be represented as latent feature vectors of a much smaller size compared to the original 2D image matrix. By comparing slices using their latent vectors, not only can we reduce the computation cost but also extract their most useful information.

We utilize an auto-encoder as the representation extractor for the slices in our 3D training image set W , which learns efficient features in an unsupervised manner and conducts

a lossy compression in the encoding process. It learns to store relevant information and disregard noise. This auto-encoder consists of two parts: An encoder produces a compressed knowledge representation x for an input image (or slice) I ; a decoder takes the representation x as input and outputs \hat{x} as a reconstruction of the original image. The entire auto-encoder model is optimized by minimizing the sum of the reconstruction error $\mathcal{L}(x, \hat{x})$, which measures the differences between the original image and the reconstruction produced, and a regularization term for alleviating overfitting. This can be formulated as:

$$
\phi^*, \psi^* = \arg \min_{\phi, \psi} (\mathcal{L}(x, \hat{x}) + \lambda_1 \times \sum_{i=1}^M w_i^2), \tag{1}
$$

where $\mathscr E$ is the reconstruction loss between x and $\hat x$, λ_1 is a scaling parameter for the where \mathcal{L} is the reconstruction loss
regularization term $\sum_{i=1}^{M} w_i^2$ to adju
overfitting, w_i is the *i* parameter of to adjust the trade-off between the sensitivity to the input and overfitting, w_i is the *i* parameter of the auto-encoder, and ϕ and ψ are the parameters of the encoder and decoder, respectively.

To facilitate a fast training and convergence of the auto-encoder, we use a ResNet-101 (He et al., 2016) pre-trained on ImageNet (Deng et al., 2009) as the encoder backbone. A light-weight decoder (ResNet-50 He et al., 2016) is added to map the latent vectors to the original input space. Since slices along each orthogonal plane will be selected, we train the auto-encoder using all the slices of the 3D training set W along the three orthogonal planes.

3.2.2. Prioritizing the slices—After training the auto-encoder, we measure the representativeness of each slice in the 3D training image set W as in Zheng et al. (2020b). First, we feed a 2D slice I to the encoder, and take the generated latent vector f as the representation of the slice I. Second, we define and compute the similarity between two slices I_i and I_j as $Sim(I_i, I_j) = cosine(f_i, f_j)$, where f_i and f_j are the latent vectors of I_i and I_j respectively, and cosine denotes cosine similarity.

Next, a subset S of slices is selected from all the slices $S(W)$ of the set W (for an annotation ratio or a given size of S). The representativeness of S with respect to W is defined as:

$$
F(S, W) = \sum_{I \in S(W)} \max_{I_s \in S} (Sim(I_s, I)).
$$
\n⁽²⁾

Finding an optimal slice subset S was formulated as a maximum cover problem in Zheng et al. (2020b), which is NP-hard, and a polynomial time approximation solution was obtained using a greedy method. Suppose a subset S' is the most representative for the images in W. The next choice (if needed) is a slice I^* in the remaining slice set $S(W) - S'$ that maximally increases the representativeness of the new subset $S' \cup \{I^*\}$, i.e.,

$$
I^* = \arg \max_{I \in (S(W) - S')} (F(S' \cup \{I\}, W) - F(S', W)).
$$
\n(3)

This selection process puts all the slices in W in decreasing order based on their representativeness. The slices with better representativeness have higher priorities for annotation.

3.3. Base-learner training and pseudo-label generation

After the representative slice selection, the selected slices are labeled by experts, which we denote as $S_L = \{S_{l_1}, S_{l_2}, ..., S_{l_N}\}\$, where l_N is the number of slices selected.

Our 2D module follows the structure of KCBAC-Net (Gu et al., 2021), since it outperforms other state-of-the-art 2D segmentation networks (e.g., UNet++ Zhou et al., 2018, TransUNet Chen et al., 2021, etc.) on our datasets in the experiments. This 2D module is a sequence of K complete bipartite networks with asymmetric convolutions, which exploits multi-scale features and enhances the capability of standard convolution on extracting discriminative features. A bipartite network structure (Chen et al., 2017), K-UNet scheme (Chen et al., 2016), asymmetric convolutions (Ding et al., 2019), and deep supervision (Lee et al., 2015) are integrated into this module.

A 2D segmentation model can have a relatively large receptive field, but it does not utilize the interactions between consecutive slices well, which may result in spatial slice-to-slice inconsistency. Hence, we follow the ensemble method in Zheng et al. (2019) and train a 3D module, which produces smoother 3D results.

We choose 3D Attention UNet (Oktay et al., 2018) as the backbone for our 3D module, since it outperforms other well-known 3D segmentation networks (e.g., 3D U-Net (Çiçek et al., 2016, DenseVoxNet Yu et al., 2017, TransUNet 3D Chen et al., 2021, UNet++ 3D Zhou et al., 2018, etc.) on our datasets in the experiments.

Similar to our 2D modules, we apply the K-UNet design (Chen et al., 2016) and build a 3D K-AttentionUNet as our 3D module to exploit 3D multi-scale features. In our 3D module of 3D K-AttentionUNet, the coarse features extracted by one AttentionUNet submodule are fed to the next AttentionUNet submodule to obtain fine-grained features.

For knee joint segmentation, the bone and cartilage boundaries are often more important than other areas, since they usually serve as the main criteria to measure whether and/or how much a cartilage is damaged. Hence, we add an edge-aware regulation to our 3D K-AttentionUNet to force the network to focus more on the object boundary areas. Fig. 4 shows the structure of our edge-aware 3D K-AttentionUNet. The edge gate $F_{L,\rho G}$ is defined as:

$$
F_{L\rho G}(I) = k_G * \rho(k_L * I), \tag{4}
$$

where k_G and k_L represent the Gaussian smoothing kernel and Laplacian kernel respectively, * denotes convolution, and ρ is an activation function.

The loss function of our 3D module is defined as:

$$
\mathcal{L} = L_{region} + \lambda_2 L_{edge}, \tag{5}
$$

where L_{region} and L_{edge} are the cross entropy losses of the region branch and edge branch respectively, and λ_2 is a scaling parameter to regularize the edge branch.

We first train our three 2D segmentation modules using the selected labeled slices for each of the three orthogonal planes, and generate the probability maps of the unlabeled slices using the three trained 2D modules. We then train our 3D edge-aware K-AttentionUNet using the 3D images in W that contain both the labeled slices and unlabeled slices that are now "labeled". Specifically, the pseudo-labels produced by the three 2D modules are first improved by the bi-HEMD algorithm in Section 3.4. Then, the probability maps attained by the three 2D modules are averaged to generate the pseudo-labels used for training our 3D module. These four trained segmentation modules generate their pseudo-labels respectively for all the unlabeled slices. For simplicity, we average the results of these four modules as the probability map for each 3D image in W .

3.4. Bi-directional hierarchical earth mover's distance

After training our three 2D modules, probability maps of all the unlabeled slices in W are obtained. One observation on the 3D knee images is that the appearances of bones and cartilages between consecutive slices are often similar in size and shape. Exploring such appearance similarity can help improve the pseudo-label quality. Hence, we apply the hierarchical earth mover's distance (H-EMD) method (Liang et al., 2022) that uses many threshold values of the probability map for each unannotated slice and exploits the appearance consistency between consecutive slices to optimize the pseudo-labels.

The H-EMD method (Liang et al., 2022) takes two key steps. (i) Candidate instance The H-EMD method (Liang et al., 2022) takes two key generation: For a set of v threshold values, $\{t_h\}_{h=1}^v$, from S_i in a 3D image, produce a set IC_i of possible object in generation: For a set of v threshold values, $\{t_h\}_{h=1}^v$, from the probability map of a slice S_i in a 3D image, produce a set IC_i of possible object instance candidates. These object candidates can be organized into a forest structure F_i . Also, a reference set R_{i-1} of object ey steps. (i) Candidate instance
om the probability map of a slice
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. Also, a reference set R_{i-1} of object
y). (ii) Candidate instance selection:
erence instance in R_{i-1} , compute The H-EMD method (Liang et al., 2022) takes two key steps. (i) Candidate instance generation: For a set of v threshold values, $\{t_h\}_{h=1}^v$, from the probability map of a slice S_i in a 3D image, produce a set IC_i o For each pair of an instance candidate in F_i and a reference instance in R_{i-1} , compute their ${t_h}_{n=1}^c$, from the probability map of a slice
ble object instance candidates. These object
ructure F_i . Also, a reference set R_{i-1} of object
iteratively). (ii) Candidate instance selection:
and a reference instan to maximize the sum of the weighted matching scores between the candidate set IC_i and instances is built on the slice S_{i-1} (obtained iteratively). (ii) Candidate instance selection
For each pair of an instance candidate in F_i and a reference instance in R_{i-1} , compute the
matching score as the cos reference set R_{i-1} to select the "best" object instances for the slice S_i . This can be solved by integer linear programming. For a dataset with n different classes, a feature vector for each instance candidate is defined as $(x, y, z, v_1, \ldots, v_n)$, whose first three items are the coordinates of its center pixel and the last *n* items are for an $n-D$ one-hot vector denoting the category of the instance.

Rather than using the Euclidean distance as in Liang et al. (2022), our method applies cosine distance, since our vectors contain two different types of information, which make the S_i distance unsuitable to measure the differences between these vectors.

Similar to the bi-directional RNN in Chen et al. (2016), we perform the H-EMD process in two opposite directions (bi-HEMD). That is, for any two labeled slices S_j and $i < j$ in a 3D image, $S_{i+1}, S_{i+2}, \ldots, S_{i-1}$, we apply H-EMD along the direction of $S_{i-1}, S_{i-2}, \ldots, S_{i+1}$, and along K . With the bi-HEMD process, the pseudo-labels generated by the 2D modules are improved, which are then used to train the 3D module in Section 3.3.

3.5. Tuning the final 3D model using pseudo-labels

We now have three 2D K-FCNs and one 3D *axial*-FCN trained with labeled or pseudolabeled slices along the *coronal*, *sagittal*, and M planes. Next, we produce the probability maps of each 3D image W in W using these four FCN modules, denoted as m_{axial} , $m_{coronal}$, $m_{sagital}$, and m_{3D} , respectively. These probability maps are averaged, and the results are used to train our 3D meta-learner. This meta-learner is a Y-shaped K-DenseVoxNet (Yu et al., 2017) that is aware of the raw images and their pseudo-labels so as to ease overfitting. Fig. 5 shows our meta-learner.

After training our 3D meta-learner, we apply the self-training strategy in Zheng et al. (2019) to further improve the model performance. In this self-training process, the segmentation results of the meta-learner are regarded as pseudo "ground truth" of the unlabeled slices, which are used to re-train the 2D/3D base-learners (the three 2D base-learners are re-trained with the "labeled" slices along the three orthogonal planes). Note that the base-learners are first trained in the step of Section 3.3. Here, we apply the SGD optimizer and a smaller learning rate to ensure the robustness and convergence of the entire training process. The loss function L_{CE} of the 3D meta-learner (see Fig. 5) is defined as the cross-entropy between the predictions and input pseudo-labels. The base-learners are re-trained, and generate four versions of pseudo-labels for each 3D image in W , which are averaged and used to train the meta-learner again. We repeat this self-training process for a few iterations, until the meta-learner performance no longer improves, giving rise to our final 3D model.

3.6. Post-processing using IPM

Instead of applying the softmax function to the final probability maps, we further perform some post-processing to fine-tune the probability maps. One observation is that the surfaces of bones and cartilages are mutually "coupled" in some areas, within which the topology and relative positions of the bones and cartilages are known and the distances between them are within specific ranges. Furthermore, physicians care more about the "coupled" areas since osteoarthritis is usually caused by damages of the knee cartilages in such areas. Thus, we apply the IPM method (Xie et al., 2022) by incorporating the surface interrelationships between the bones and cartilages into the segmentation process to further improve the segmentation performance. An advantage of the IPM method over traditional graph based methods is that it parameterizes the surface cost functions in the graph model and leverages DL to learn the parameters rather than relying on hand-crafted features.

Instead of using ground truth to train the surface segmentation network of IPM (Xie et al., 2022), we use the pseudo-labels generated by our meta-learner to optimize this network in the first iteration. Afterwards, the pseudo-labels are updated by IPM and used to re-train the

network. Such operations are repeated several times until convergence. The details of the above training process are shown in Fig. 7 (Xie et al., 2022).

Since the bone and cartilage surfaces are not terrain-like, we need to first unfold the knee joint into seven parts following the practice in Zhou et al. (2019), i.e., the front, back, top, center, bottom, left and right parts, respectively, as shown in Fig. 6.

Specifically, for the center part (see Fig. 6(d)), we replace U-Net used in the original IPM method (Xie et al., 2022) with the probability maps generated by our final fine-tuned ensemble model. Finally, we patch its 6 junction areas (i.e., the junction areas between center and front, center and back, center and top, center and bottom, center and left, and center and right), and average the center area and its corresponding junction areas processed by IPM to smooth the final results.

4. Experiments and analysis

To demonstrate the capabilities of our KCB-Net approach, its performance was compared with state-of-the-art knee segmentation methods using full annotations as well as compared with two state-of-the-art slice selection strategies: equal-interval annotation (EIA) and random slice selection (RSS). Furthermore, the effect of each component in our KCB-Net framework was assessed and the robustness of the method was quantified for different sparse annotation ratios.

4.1 Datasets and implementation details

Our experiments use four 3D MR knee joint datasets, the SKI10 dataset, OAI ZIB dataset, Iowa dataset, and iMorphics dataset, which we describe below.

The SKI10 Dataset—This dataset contains 60 3D MR images for training, 40 for validation, and 50 for testing, from the MICCAI SKI10 challenge. The images were from the surgical planning program of Biomet, Inc., and were annotated by experts. It only covers the time-point of baseline. Four compartments were annotated: femural bone (FB), femural cartilage (FC), tibia bone (TB), and tibia cartilage (TC). More details of this dataset can be found in Heimann et al. (2010).

The OAI dataset—Three sub-datasets, the OAI ZIB dataset, iMorphics dataset, and Iowa dataset, from the OAI dataset are used to evaluate the performance of our KCB-Net. The images of these three sub-datasets were from the Osteoarthritis Initiative database (OAI, <http://www.oai.ucsf.edu/>). (1) The OAI ZIB dataset consists of 507 3D MR images annotated by experts of the Zuse Institute Berlin. It only covers the time-point of baseline. The details of this dataset are depicted in Ambellan et al. (2019). (2) The iMorphics dataset (Bowes et al., 2015), available directly from the OAI database, includes 176 3D MR knee images acquired with 3T Siemens MAGNETOM Trio scanners and quadrature transmit– receive knee coils (USA Instruments, Aurora, OH, USA). The annotated compartments are femoral cartilage (FC), tibia cartilage (TC), patellar cartilage (PC), and menisci (M). It covers the time-point of baseline and 12 month follow-up. (3) The Iowa dataset, a University of Iowa annotated portion of the OAI dataset that was first segmented by the LOGISMOS

method (Kashyap et al., 2017) and the automatic segmentations were then corrected by the just-enough-interaction (JEI) approach in $4D(3D + time)$ (Zhang et al., 2020). The Iowa dataset consists of 1462 double echo steady state (DESS) 3D MR images from 248 subjects. Four compartments were annotated: femur bone (FB), femoral cartilage (FC), tibia bone (TB), and tibial cartilage (TC). Different time-points were covered by this dataset: some subjects were covered with baseline and 12 month follow-up, and some were covered with baseline, 12, 24, 30, 36, 48, 72, and 96 month follow-ups.

We implemented all the tested networks using PyTorch (Paszke et al., 2019). For our autoencoder, ResNet-101 (He et al., 2016) is used as the backbone of its encoder and ResNet-50 (He et al., 2016) as the backbone of its decoder. The encoder is initialized with a model pre-trained on ImageNet (Deng et al., 2009). All the other parameters are initialized as in He We implemented all the tested networks using PyTorch (Paszke et al., 2019). For our auto-
encoder, ResNet-101 (He et al., 2016) is used as the backbone of its encoder and ResNet-5
(He et al., 2016) as the backbone of its encoder, Resivet-101 (Fig. et al., 2016) is used as the backbone of its encoder and Resivet-50.
(He et al., 2016) as the backbone of its decoder. The encoder is initialized with a model
pre-trained on ImageNet (Deng et al as to remove the background clearly outside of the knee area. Each slice or 3D image was normalized to zero mean and unit standard variance. In the data augmentation for 3D model training, starting points are randomly selected in a 3D image, and a patch of size $80 \times 192 \times$ 160 is cropped at each starting point, making sure that the cropped patch locates completely inside the 3D image. Afterwards, common spatial transforms (e.g., rotation, scaling, and mirroring) are applied. In 2D model training, each slice is augmented with common spatial transforms. inside the 3D image. Afterwards, common spatial transforms (e.g., rotation, scaling, and
mirroring) are applied. In 2D model training, each slice is augmented with common spatial
transforms.
We set $K = 2$ for the KCBAC-Ne

larger K, the model costs increase largely but the accuracy improves little Chen et al., 2016). We use *mean square error* as the auto-encoder's loss. We set the parameter of the edge regularizer in the edge-aware 3D K-AttentionUNet as $\lambda_2 = 1e - 4$ (see Eq. (5)).

4.2. Evaluation metrics

The following evaluation metrics are used in our experiments and comparisons.

4.2.1. Dice similarity coefficient—Dice similarity coefficient (DSC) is calculated as:

$$
DSC = \frac{2 \times V(GT \cap Pred)}{V(GT) + V(Pred)},
$$
\n(6)

 $DSC = \frac{2 \times V(GT \cap Pred)}{V(GT) + V(Pred)},$
where GT is the ground truth, *Pred* is the prediction, and $V(X)$ denotes the volume of a 3D object X. object X.

4.2.2. Average symmetric surface distance—Average symmetric surface distance (ASSD) focuses on the absolute distances between surfaces of the segmented objects and their ground truths, calculated as:

$$
ASSD = \frac{1}{n\partial A + n\partial B} \left(\sum_{a \in \partial A} d(a, \partial B) + \sum_{b \in \partial B} d(b, \partial A) \right),\tag{7}
$$

where ∂A and ∂B denote the surfaces of objects A and B respectively, n ∂A and n ∂B denote Page 11
where ∂A and ∂B denote the surfaces of objects A and B respectively, $n\partial A$ and $n\partial B$ denote
the numbers of voxels on ∂A and ∂B respectively, and $d(x, \partial S)$ denotes the nearest Euclidean distance of a point x to a surface ∂S .

4.2.3. Root Mean Square symmetric surface distance—Root Mean Square symmetric surface Distance (RMSD) is a variation of ASSD, except that all the distances are squared first and the root is conducted for the average value. RMSD is computed as:

$$
RMSD = \sqrt{\frac{1}{n \partial A + n \partial B}} \left(\sum_{a \in \partial A} d(a, \partial B)^2 + \sum_{b \in \partial B} d(b, \partial A)^2 \right),\tag{8}
$$

in which all the terms are defined as in Eq. (7). In RMSD, a larger deviation is penalized stronger. This metric is used for comparison with previous methods on the SKI10 dataset.

4.2.4. Volume overlap error—The volume overlap error (VOE) between the GT and Pred is calculated as:

$$
VOE = 1 - \frac{V(GT \cap Pred)}{V(GT \cup Pred)}.
$$
\n(9)

A smaller value of VOE means a better segmentation, with 0 for perfect segmentation and 1 for no overlap of GT and Pred at all. This metric is used for comparison with previous methods on the SKI10 dataset.

4.2.5. Volume difference—The volume difference (VD) between the GT and Pred is calculated as:

$$
VD = \frac{V(Pred) - V(GT)}{V(GT)}.
$$
\n(10)

VD is used in the scoring of cartilages on the SKI10 dataset. It approximately indicates the deviation from the average cartilage thickness when the evaluation is limited on the respective ROIs.

4.3. Experimental results with full annotation

To evaluate the effectiveness of our approach, we compare the performance of KCB-Net with the following recent methods on the SKI10 dataset and ZIB dataset with full annotation. (i) CNN-SSM: integrating CNN with a statistical shape model (Ambellan et al., 2019). (ii) The ensemble method (Zheng et al., 2020b). (iii) UNet++ 3D (Zhou et al., 2018). (iv) Attention UNet 3D (Oktay et al., 2018). (v) TransUNet 3D (Chen et al., 2021). For fair comparison, we follow the dataset split strategy in Ambellan et al. (2019) and use the evaluation metrics in Heimann et al. (2010).

Tables 1 and 2 present the performance comparisons of our KCB-Net with the other methods trained on the SKI10 dataset and OAI ZIB dataset with full annotation, respectively. From Table 1, one can see that our KCB-Net outperforms the best-known method, CNN-SSM, in

all the metrics except the ASSD on femoral bone and tibial bone. Our overall score on the SKI10 dataset is higher by 1.94 than that of CNN-SSM.

To further examine the robustness of our KCB-Net, five-fold cross validation is conducted on the four datasets. Note that for the SKI10 dataset, some of the utilized evaluation metrics require the ROIs of the femur and tibial areas, which are not available in some cases; thus, we compare KCB-Net in the commonly used DSC and ASSD metrics with the other methods. We split a whole dataset in the ratio of 7:1:2, corresponding to training, validation, and testing, for each fold on the four datasets using stratification by subject IDs. The final results are the averages of the five folds, which are given in Tables 3, 4, 5, and 6, respectively. As Tables 3 and 4 show, our approach achieves the best results on the SKI10 and OAI ZIB datasets.

Table 5 shows the performance comparison of our KCB-Net and the other methods trained on the fully annotated Iowa dataset. The Iowa dataset was used for comparison with the following known methods. (i) 4D LOGISMOS (Kashyap et al., 2017): utilizing a hierarchical set of random forest classifiers to learn the cartilage appearance and simultaneously segment multiple interacting surfaces of objects based on an algorithmic incorporation of multiple spatial interrelationships in an n -dimensional graph. (ii) CML (Tan et al., 2019): detecting the regions of interest and fusing the cartilages by a fusion layer. Since we could not access the source code of the original method, we implemented the approach and applied it to the Iowa dataset. The hyper-parameters (e.g., the number of filters, down-samplings, and up-samplings) used in our implementation are the same as presented in the original paper. We experimented with both the 2D and 3D versions of CML, which showed that the 2D version yielded better results on the Iowa dataset. (iii) The ensemble learning method (Zheng et al., 2020b): Ensembling four 2D/3D FCNs and self-training with fully labeled 3D data. (iv) UNet++ 3D (Zhou et al., 2018). (v) Attention UNet 3D (Oktay et al., 2018). (vi) TransUNet 3D (Chen et al., 2021).

From Table 5, one can see that our KCB-Net outperforms LOGISMOS-4D on both the femoral and tibial cartilage segmentations. KCB-Net also outperforms the ensemble method (Zheng et al., 2020b), which demonstrates that the KCBAC-Net based 2D modules, K-UNet design, edge-aware 3D AttentionUNet, bi-HEMD method, and IPM post-processing method that we use in KCB-Net help improve the segmentation performance.

Table 6 presents the results achieved on the fully annotated iMorphics dataset. We compare with the following recent methods. (i) UDA (Panfilov et al., 2019): utilizing mixup and adversarial unsupervised domain adaptation to improve the robustness of DL-based knee cartilage segmentation in new MRI acquisition settings. (ii) CML (Tan et al., 2019). (iii) The ensemble method (Zheng et al., 2020b). (iv) UNet++ 3D (Zhou et al., 2018). (v) Attention UNet 3D (Oktay et al., 2018). (vi) TransUNet 3D (Chen et al., 2021). Our method attains better DSC scores on FC, TC, PC, and M compared to the UDA method. We also outperform the CML and ensemble methods in both DSC and surface errors of FC, TC, PC, and M, suggesting that our method can obtain more quantitatively accurate knee cartilage and bone segmentations.

Performance improvement of our KCB-Net over the original ensemble method (Zheng et al., 2020b) was evaluated on the four datasets, using paired t-tests. Tables 1, 2, 3, 4, 5, and 6 show that in most of the compared cases, our new approach significantly outperforms the ensemble approach (Zheng et al., 2020b) (with p -values < 0.05).

4.4. Experimental results with sparse annotation

To evaluate the effectiveness of our approach on sparsely annotated data, we compare its performances on the four datasets with changing sparse annotation ratios vs. those achieved using different slice selection schemes. Specifically, we compare the representative annotation (RA) scheme used in our KCB-Net pipeline with two common slice selection schemes: equal-interval annotation (EIA) and random slice selection (RSS).

Suppose for a specified annotation ratio, S_k slices are to be selected. The EIA scheme annotation (RA) scheme used in our KCB-Net pipeline with two common slice selection
schemes: equal-interval annotation (EIA) and random slice selection (RSS).
Suppose for a specified annotation ratio, S_k slices are to b schemes: equal-interval annotation (EIA) and random slice selection (RSS).
Suppose for a specified annotation ratio, S_k slices are to be selected. The EIA scheme
selects S_k / 3 slices at equal distance along each axis of the results as the RSS-based performance. 8, Figs. 9, 10, and 11 show the performance comparisons with various annotation ratios on the SKI10, OAI ZIB, iMorphics, and Iowa datasets, respectively.

Figs. 8, 9, 10, and 11, one can see that our RA outperforms the EIA and RSS schemes on both the cartilage and bone segmentations in most the cases. Our method can notably alleviate performance degradation, especially for annotation ratios ≤30%. This is because EIA selects the locationally same slice indices in each 3D image, which might make the trained model overfit on the selected slices of the same indices and cause segmentation errors on the remaining slices. RSS performs better than EIA in very sparse annotation ratios (10%–30%) for most of the segmentation targets but sometimes performs worse than EIA in less sparse annotation ratios (e.g., >50%), since RSS can select different slices in different 3D images, likely incurring less overfitting. The performances of these three selection schemes are similar for annotation ratios >80% since many slices they select tend to be the same or similar at such dense annotation ratios.

Another observation from these four figures is that the performance drops quickly when the annotation ratios are <30% for most of the segmentation targets, suggesting that the annotation ratio of 30% might be a "lower limit" for a satisfactory performance for knee segmentation.

4.5. Ablation study

To examine the contribution of each key component in our KCB-Net, we conducted an ablation study to evaluate the performances of its components, denoted as follows. (1) SI: 2D axial module; (2) S2: 2D coronal module; (3) S3: 2D sagittal module; (4) S4: 3D module; (5) S5: ensembling of the three 2D modules and the 3D module; (6) S6: bi-HEMD; (7) S7: self-training; (8) S8: IPM post-processing.

The performance of each individual component in S1, S2, S3, and S4 is given first, followed by the ensemble performance (S5) that combines all these four components. For S6–S8, components are sequentially added to the framework each time; the more the performance

increases, the more contribution the corresponding component (in S6–S8) makes. Thus, note that S8 actually reflects the performance of the entire framework including all its components.

7, 8, 9, and 10 present the ablation study results on the SKI10, OAI ZIB, iMorphics, and Iowa datasets, respectively. We observe that the ensemble of the 2D and 3D modules can substantially improve the performance over the individual modules. The 3D module often attains better performance than the 2D modules since it exploits the interrelations among consecutive slices. The ensemble strategy can benefit from both the 2D modules (with a large receptive field) and the 3D module (exploiting the interactions among consecutive slices). Since some cartilages are very thin along the sagittal plane, it is quite difficult for DL models to detect them along one such plane, especially with very sparse annotation. Utilizing other 2D modules can help address this issue. Tables 7, 8, 9, and 10 show that the ensemble strategy and the self-training mechanism play more important roles than the other components. Figs. 12 and 13 qualitatively compare results in the sagittal view on the Iowa and iMorphics datasets.

4.6. Discussion

From Figs. 8, 9, 10, and 11, one can see that our representative annotation (RA) scheme substantially reduces the performance gap between different sparse annotation ratios and full annotation, suggesting that our framework can achieve comparatively good results while using much less annotated data than required for full annotation. Our ensemble method and the self-training scheme using pseudo-labels improved by the bi-HEMD method largely improve the segmentation performance, because the training data we use contribute more information in an efficient way. Figs. 12 and 13 show that our ensemble and self-training strategies allow detection of small objects and thin boundary areas, despite the annotation sparsity. Our IPM post-processing helps further fine-tune the object boundary areas, making the overall segmentation results more accurate and reliable.

5. Conclusions

We reported a new framework, KCB-Net, for segmenting cartilages and bones in 3D knee joint MR images. Our method efficiently selects subsets of diverse image slices for expert annotations in a way that the most information-contributing slices are ranked most highly, allowing to train image segmentation models using high-sparsity ratio annotations. In the KCB-Net, three 2D segmentation modules and one 3D module integrating features across multiple scales with edge-aware branches are ensembled to generate pseudo-labels of the un-annotated slices, which are then used to re-train the 3D model. An IPM process is employed to post-process the probability maps generated by the 3D model. Experiments on four large knee datasets show that our new approach outperforms state-of-the-art methods on fully annotated datasets, and can notably improve segmentation performances when annotating only small data subsets.

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Fig. 1.

Knee joint. (a) Anatomy of the knee joint (adopted from Paley Orthopedic & Spine Institute (2018)). (b)–(d) Sagittal, coronal, and transverse MR image planes, showing the femur bone (FB), femoral cartilage (FC), tibia bone (TB), tibial cartilage (TC), patella bone (PB), patellar cartilage (PC), and meniscus (M).

Fig. 2.

The pipeline of our proposed KCB-Net framework.

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Fig. 4.

box denotes a 3D AttentionUNet block.

Fig. 5. The structure of our meta-learner.

Fig. 6.

Illustrating the seven unfolded parts of the knee joint. The corresponding parts in the sagittal view are: (a) front; (b) back; (c) top; (d) center; (e) bottom; (f) left; (g) right.

The process of the post-processing step (Xie et al., 2022).

Fig. 9.

Comparison of the three slice selection schemes (RA, EIA, and RSS) on the OAI ZIB dataset.

Fig. 10.

Comparison of the three slice selection schemes (RA, EIA, and RSS) on the iMorphics dataset.

Fig. 12.

Visual comparison of knee bone and cartilage segmentation by our KCB-Net and Attention UNet 3D (a best-known 3D segmentation method) in the sagittal view on the Iowa dataset. (a) An input 2D slice from a 3D image; (b) segmentation ground truth; (c) segmentation by Attention UNet 3D; (d) segmentation by our KCB-Net. Our KCB-Net is able to correctly segment some thin boundary areas (e.g., see the dashed yellow boxes).

Fig. 13.

Visual comparison of knee bone and cartilage segmentation by our KCB-Net and Attention UNet 3D (a best-known 3D segmentation method) in the sagittal view on the iMorphics dataset. (a) An input 2D slice from a 3D image; (b) segmentation ground truth; (c) segmentation by Attention UNet 3D; (d) segmentation by our KCB-Net. Our KCB-Net is able to correctly segment some small cartilage areas (e.g., see the dashed red and blue boxes).

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Table 1

metrics used in Heimann et al. (2010). Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble metrics used in Heimann et al. (2010). Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble Comparison with state-of-the-art methods using full annotation on the SKI10 dataset following the data split in Ambellan et al. (2019) and evaluation Comparison with state-of-the-art methods using full annotation on the SKI10 dataset following the data split in Ambellan et al. (2019) and evaluation method (Zheng et al., 2020b). method (Zheng et al., 2020b).

Marks the row in which the results are from the original paper. Marks the row in which the results are from the original paper.

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Table 2

Comparison with state-of-the-art methods using full annotation on the OAI ZIB dataset following the data split in Ambellan et al. (2019). Paired t-test Comparison with state-of-the-art methods using full annotation on the OAI ZIB dataset following the data split in Ambellan et al. (2019). Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b). values indicate the significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b).

 ${}^{\rm 2}\!{\rm M}$ arks the row in which the results are from the original paper. Marks the row in which the results are from the original paper.

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Table 3

Comparison with state-of-the-art methods using full annotation on the SKI10 dataset with five-fold cross validation. Paired t-test values indicate the Comparison with state-of-the-art methods using full annotation on the SKI10 dataset with five-fold cross validation. Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b). significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b).

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Table 4

Comparison with state-of-the-art methods using full annotation on the OAI ZIB dataset with five-fold cross validation. Paired t-test values indicate the Comparison with state-of-the-art methods using full annotation on the OAI ZIB dataset with five-fold cross validation. Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b). significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b).

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Table 5

Comparison with state-of-the-art methods using full annotation on the Iowa dataset. Paired t-test values indicate the significance status of the improved Comparison with state-of-the-art methods using full annotation on the Iowa dataset. Paired t-test values indicate the significance status of the improved performance of our method vs. the ensemble method (Zheng et al., 2020b). "-" denotes that the corresponding results were not reported in the original performance of our method vs. the ensemble method (Zheng et al., 2020b). "–" denotes that the corresponding results were not reported in the original paper.

²Marks the row in which the results are from the original paper. Marks the row in which the results are from the original paper.

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Table 6

improved performance of our method vs. the ensemble method (Zheng et al., 2020b). "-" denotes that the corresponding results were not reported in the improved performance of our method vs. the ensemble method (Zheng et al., 2020b). "–" denotes that the corresponding results were not reported in the Comparison with state-of-the-art methods using full annotation on the iMorphics dataset. Paired t-test values indicate the significance status of the Comparison with state-of-the-art methods using full annotation on the iMorphics dataset. Paired t-test values indicate the significance status of the original paper. original paper.

 ${}^{\rm 2}$ Marks the rows in which the results are from the original papers. Marks the rows in which the results are from the original papers.

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Ablation study of our method on the SKI10 dataset. Ablation study of our method on the SKI10 dataset.

Ablation study of our method on the OAI ZIB dataset. Ablation study of our method on the OAI ZIB dataset.

Ablation study of our method on the iMorphics dataset. Ablation study of our method on the iMorphics dataset.

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Ablation study of our method on the Iowa dataset. Ablation study of our method on the Iowa dataset.

