Learning from Multiple Datasets with Heterogeneous and Partial Labels for Universal Lesion Detection in CT

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Abstract—Large-scale datasets with high-quality labels are desired for training accurate deep learning models. However, due to annotation costs, medical imaging datasets are often either partially-labeled or small. For example, DeepLesion is a large-scale CT image dataset with lesions of various types, but it also has many unlabeled lesions (missing annotations). When training a lesion detector on a partially-labeled dataset, the missing annotations will generate incorrect negative signals and degrade performance. Besides DeepLesion, there are several small single-type datasets, such as LUNA for lung nodules and LiTS for liver tumors. Such datasets have heterogeneous label scopes, i.e., different lesion types are labeled in different datasets with other types ignored. In this work, we aim to tackle the problem of heterogeneous and partial labels, and develop a universal lesion detection algorithm to detect a comprehensive variety of lesions. First, we build a simple yet effective lesion detection framework named Lesion ENSemble (LENS). LENS can efficiently learn from multiple heterogeneous lesion datasets in a multi-task fashion and leverage their synergy by feature sharing and proposal fusion. Next, we propose strategies to mine missing annotations from partially-labeled datasets by exploiting clinical prior knowledge and cross-dataset knowledge transfer. Finally, we train our framework on four public lesion datasets and evaluate it on 800 manually-labeled sub-volumes in DeepLesion. On this challenging task, our method brings a relative improvement of 49% compared to the current state-of-the-art approach.

Index Terms—Lesion detection, multi-dataset learning, partial labels, heterogeneous labels, noisy labels.

I. INTRODUCTION

TRAINING datasets play a key role in data-driven deep learning algorithms for medical image analysis. Different from natural images, annotating medical images demands extensive clinical expertise, making it difficult to acquire large-scale medical image datasets with complete and high-quality labels. A possible solution is to train on multiple datasets to integrate their knowledge [1]–[7]. Compared to training a separate model on each dataset, joint training offers three advantages: first, the size of training data is expanded without further manual annotation; second, training and inference become more efficient, as multiple models are consolidated into a single model [1]; and third, the combined training data cover a larger distribution (e.g., different datasets come from different hospitals), potentially increasing the generalizability of the trained model [4]. The main challenge of this strategy is that the label scope of different datasets is often heterogeneous. For example, in chest X-ray disease classification, the label set is not identical across datasets [9], [10], [11]. In multi-organ segmentation, varying organs are labeled in different datasets [2], [3], [6]. Even if a label is shared between two datasets, its definition may vary due to different data collection and annotation criteria (concept shift) [5]. Therefore, combining multiple datasets is not straightforward and may degrade accuracy if the above problems are not solved properly [2].

Another method to address data scarcity is to collect images and labels by data mining [8], [9]. This strategy can produce large-scale datasets with minimal manual effort, but at the cost of imperfect mined labels. Taking DeepLesion [9], [10] as an example, it was collected by mining lesion annotations directly from the picture archiving and communication system (PACS), which stores the lesion marks [11] produced by radiologists during their routine work. DeepLesion includes over 32K lesions of various body parts in computed tomography (CT) scans. Despite its large scale, DeepLesion has a limitation: not all lesions in every slice were annotated. This is because radiologists generally mark only representative lesions in each scan subjectively in their routine work [11]. This missing annotation or partial label problem will cause incorrect training signals (some negative proposals are actually positive), resulting in a lower detection accuracy.

In this paper, we tackle the heterogeneous and partial label problem in multi-source deep learning for the purpose of improved lesion detection. As a major task in medical image analysis, lesion detection aims at assisting radiologists to locate abnormal image findings, decrease reading time and improve accuracy/sensitivity [12], [13]. Existing lesion detection works commonly focus on lesions of specific types and organs. For example, lung nodules [13]–[15], liver tumors [17], and lymph nodes [18]–[20] have been extensively studied. However, in real clinical scenarios, a CT scan may contain multiple types of lesions in different organs. For instance, metastasis (e.g., lung cancer) can spread to regional lymph nodes and other body parts (e.g., liver, bone, adrenal, etc.). Clinicians need to locate all types of findings to determine the patient’s tumor stage and future treatment [11]. The
Our first goal is to improve ULD by learning from multiple lesion datasets. Existing works on ULD [17], [22], [25] learned from the DeepLesion dataset alone. In this work, we make one step forward to also leverage other public single-type lesion datasets [14], [26], [27], which provide annotations of specific lesion types. Fig. 1 shows exemplar labels in different lesion datasets. To deal with the label scope difference and concept shift aforementioned, we propose a simple yet effective multi-dataset lesion detection framework. It includes multiple dataset-specific anchor-free proposal networks and a multi-task detection head. Given an image, our algorithm can predict several groups of lesion proposals that match the semantics of each dataset. It can be considered as an ensemble of “dataset experts”, thus is named Lesion ENSemble (LENS). After this step, a patch-based 3D lesion classifier is used to further reduce false positives.

We first train LENS on all datasets to generate lesion proposals on the training set of DeepLesion, and then mine missing annotations from them to mitigate the partial label problem. We use cross-slice box propagation to extend existing 2D annotations to 3D. Next, we propose an intra-patient lesion matching strategy to mine lesions that are annotated in one scan but missed in another scan of the same patient, leveraging the prior knowledge that the same lesion instance exists across scans of the same patient. An embedding-based retrieval method is adopted for matching. Lastly, we propose a cross-dataset lesion mining strategy to find more uncertain lesions with the help of single-type dataset experts in LENS. The mined missing annotations and uncertain lesions are incorporated to retrain LENS for performance improvement. These strategies also enable us to mine lesions from the abundant unlabeled images in DeepLesion [9], [10] and then leverage them during training.

In our framework, knowledge in multiple datasets are integrated in three levels: 1) different datasets share the network backbone of LENS to learn better feature representation from multi-source CT images; 2) the lesion proposals of multiple dataset experts in LENS are fused to improve the sensitivity of ULD; 3) single-type datasets help to mine missing annotations in partially-labeled datasets to improve the quality of training labels. We employ DeepLesion and three single-type datasets in our framework, namely LUNA (LUNG Nodule Analysis) [14], LiTS (Liver Tumor Segmentation Benchmark) [27], and NIH-LN (NIH Lymph Node) [26]. For evaluation, all lesions in 800 sub-volumes in DeepLesion are manually annotated by a board-certified radiologist as the test set. On this task, our LENS trained on multiple datasets outperforms the current single-dataset state-of-the-art method [25] in average sensitivity (from 33.9% to 39.4%). After adding the mined lesions, the sensitivity is further improved to 47.6%. It is not our goal to achieve new state-of-the-art results on the single-type lesion datasets. Nevertheless, we found that LENS jointly trained on 4 datasets can achieve comparable or better accuracy on each dataset relative to the baselines trained on each dataset alone, and significantly outperformed the baselines when the number of training images is small.

The main contributions of this paper are summarized as follows: 1) The large-scale heterogeneous dataset fusion problem in lesion detection is tackled for the first time via our LENS network. 2) We propose two novel strategies, i.e. intra-patient lesion matching and cross-dataset lesion mining, to alleviate the missing annotation problem and improve lesion detection performance. 3) Knowledge is integrated across datasets through feature sharing, proposal fusion, and annotation mining. 4) The ULD accuracy on DeepLesion [9] is significantly improved upon previous state-of-the-art work [25], under a more clinically realistic 3D lesion detection setup (on 800 completely-labeled CT sub-volumes), instead of only finding lesions anchored on key slices [25].

II. RELATED WORK

Universal lesion detection: Convolutional neural networks (CNNs), such as Faster R-CNN [28] and Mask R-CNN [29], are widely used in lesion detection. Based on these detection networks, ULD has been improved by researchers using 3D context fusion [17], [22], [25], attention mechanism [17], [23], [24], multi-task learning [23], [25], and hard negative mining [30]. 3D context information in neighboring slices is

1 We were unable to annotate full volumes, since images in DeepLesion were released in sub-volumes containing 7~220 consecutive slices.
important for detection, as lesions may be less distinguishable in just one 2D axial slice. Volumetric attention [17] exploited 3D information with multi-slice image inputs and a 2.5D network to obtain top results on the LiTS dataset. In [17], [24], attention mechanisms were applied to emphasize important regions and channels in feature maps. The multi-task universal lesion analysis network (MULAN) [25] achieved the state-of-the-art accuracy on DeepLesion with a 3D feature fusion strategy and joint learning of lesion detection, segmentation, and tagging tasks. However, it did not handle the missing annotations. ULDor [30] used a trained detector to mine hard negative proposals and then retrained the model, but the mined negatives may actually contain positives because of missing annotations. None of the above methods can deal with multiple datasets with heterogeneous labels.

**Multi-task and multi-dataset learning:** To increase training data, reduce overfitting, and improve accuracy, researchers have tried to learn from multiple datasets labeled by different medical institutes using varying criteria [1]. In chest X-ray classification, it is found that joint training on multiple datasets leads to better performance [7], [31]. Cohen et al. [5] observed that the same class label had different distributions (i.e., concept shift) among multiple chest X-ray datasets and simply pooling all datasets is not optimal. Luo et al. [4] applied model ensemble to mine missing labels in heterogeneous datasets. In multi-organ segmentation, Zhou et al. [3] and Dmitriev et al. [6] tried to learn multi-organ segmentation from single-organ datasets, incorporating priors on organ sizes and dataset-conditioned features, respectively. Although multi-dataset learning is receiving increasing attention in classification and segmentation tasks in medical imaging, it has not been adequately studied in lesion detection. The domain-attentive universal detector [23] used a domain attention module to jointly learn DeepLesion and 10 natural object datasets. Yet, it did not exploit the semantic overlap between datasets. Our framework leverages the synergy of multiple lesion datasets to not only learn shared features, but also utilize their semantic overlaps for proposal fusion and annotation mining.

**Learning with partial labels:** In detection, knowledge distillation [32] can help to find missing annotations. The basic idea is to treat the predicted boxes of a model as new annotations. In [33], predictions from multiple transformations of unlabeled data were merged to generate new training annotations. Prior knowledge can also help to infer reliable missing annotations. Jin et al. [34] mined hard negative and positive proposals from unlabeled videos based on the prior that object proposals should be continuous across frames. Niitani et al. [35] introduced part-aware sampling based on the fact that an object (car) must contain its parts (tire). Wang et al. [36] propagated 2D annotations to adjacent slices to mine missing annotations in DeepLesion. In our framework, besides applying a similar strategy as [36], we also exploit prior knowledge of intra-patient lesion correspondence and cross-dataset knowledge distillation to find reliable and uncertain missing annotations.

### III. Method Overview

Our lesion detection framework combines multi-dataset learning with missing annotation mining. The former generates lesion proposals as the basis of the latter, while the latter provides refined labels to retrain the former. It consists of five main steps, which we will introduce in Sections IV and V.

1. Train LENS on all datasets using existing annotations.
2. Generate multi-dataset proposals on the training set of the partially-labeled datasets.
3. Mine missing annotations and uncertain lesions from the generated proposals.
4. Retrain LENS with the missing annotations as additional ground-truths and uncertain ones as ignored regions.
5. Use the true positive and false positive proposals of LENS to train a classifier for false positive reduction.

### IV. Multi-dataset Lesion Detection

The proposed detection framework is exhibited in Fig. 2. It consists of a two-stage detection network and a classification network for false positive reduction. The detection network, Lesion Ensemble (LENS), contains a shared backbone, multiple simple yet effective anchor-free proposal networks, and a multi-task detection head.

#### A. Backbone

We make different datasets share the network backbone of LENS to learn better feature representation from multi-source CT images. Similar to [25], we use a 2.5D truncated DenseNet-121 [37] with 3D feature fusion layers and a feature pyramid network (FPN) [38] as the backbone. The detailed structure of the backbone can be found in [25]. We tried to apply domain adaptation layers [23], [39] in multi-domain learning literature, but no accuracy improvement was found. This is probably because all datasets we used are CT images with small difference in the image domain, while [23], [39] were designed for very different images.

#### B. Anchor-Free Proposal Network (AFP)

Anchor-free detectors [40]–[42] do not need manually tuned anchor sizes [28], thus are convenient particularly when multiple datasets have different size distribution. Our proposed anchor-free proposal network (AFP) is displayed in Fig. 2. Inspired by [40]–[42], we use a centerness branch and a box regression branch to predict each pixel in the feature map. Both branches include two convolutional layers and a ReLU layer. The centerness branch predicts whether a pixel is in the center region of a lesion. Denote a ground-truth lesion box as $B = (x, y, w, h)$ where $(x, y)$ is its center and $(w, h)$ its width and height. We define $B_{ign} = (x, y, r_w, r_h)$ and $B_{ign} = (x, y, r_w, r_h)$, thus $B_{ign}$ and $B_{ign} - B_{ign}$ are the lesion’s center region and ignored region, respectively. In Fig. 2 the white and gray areas indicate the center region and the ignored region of a lesion box, respectively. We use $r_w = 0.2, r_i = 0.5$ in this paper [42]. The centerness branch is required to predict 1 in $B_{ign}$ and 0 in everywhere else except the ignored region. If a lesion box is marked as
uncertain (see Sec. V-C), it will only have $B_{\text{gt}}$ and have no $B_{\text{cn}}$ so as to be entirely ignored. The focal loss \cite{lin2017focal} is adopted to supervise the centerness branch. The box regression branch predicts four values for each pixel, namely the distance between the pixel and the left, right, top, and bottom borders of the lesion box, respectively. It uses the L1 loss \cite{lin2017focal}, which is only computed in $B_{\text{cn}}$ of each ground-truth. During inference, a box is predicted on each pixel according to the four regressed values with the objectness score predicted by the centerness branch.

C. Lesion Ensemble (LENS)

In our problem, multiple lesion datasets have heterogeneous labels. A lesion type may be annotated in dataset $i$ but not in $j$. Therefore, it is suitable to learn them in a multi-task fashion \cite{li2019joint}. LENS includes $d$ dataset-specific AFPs (Fig. 2), where $d$ is the number of datasets. We pool the proposals from all AFPs, do non-maximum suppression (NMS), and then feed them to an ROIAlign layer \cite{he2017mask} and a detection head. The detection head includes two fully connected (FC) layers that are shared across datasets, followed by dataset-specific classification layers and box regression layers to predict the detection score $s$ (lesion vs. non-lesion) and box offsets $\Delta$ \cite{lin2017focal} for each proposal. Essentially, we first merge the proposals of all AFPs to generate a comprehensive set of dataset-agnostic and universal lesion proposals, then do dataset-specific rescoring in the detection head to output boxes matching each dataset’s semantics. Note that a dataset-specific AFP or detection layer is updated only when the training data comes from the corresponding dataset. The overall loss function of LENS is

$$L = \sum_{i=1}^{d} \sum_{j=1}^{n_i} L_{ij}^{\text{center}} + \lambda_1 L_{ij}^{\text{size}} + \lambda_2 L_{ij}^{\text{class}} + \lambda_3 L_{ij}^{\text{box}},$$

where $n_i$ is the number of training samples in dataset $i$; $L_{ij}^{\text{center}}$ and $L_{ij}^{\text{size}}$ are the losses for the centerness and box regression branches of AFP$_i$, respectively; $L_{ij}^{\text{class}}$ and $L_{ij}^{\text{box}}$ are the losses for the $i$th classification and box regression layers of the detection head, respectively. $\lambda_1$ and $\lambda_2$ are the loss weights, which we empirically set as 0.1 and 10 in this paper. In inference, the multi-task detection head of LENS can generate multiple groups of lesion proposals to match the semantics of each dataset for each test image. It can be considered as an ensemble of “dataset experts”. This is more efficient than training a separate model for each dataset and run every model during inference. Our experiments demonstrate that the accuracy on each dataset is comparable or improved owing to joint training, especially for small datasets.

An important finding is that the predictions of dataset experts are complementary. As shown in Fig. 3 the single-type experts often performs better in their specialties compared to the universal dataset expert. This is mainly because their training datasets are fully-labeled and include more hard cases. On the other hand, the single-type experts cannot detect other lesion types (Fig. 3 (f)). Even if the lesion is in the same organ of their specialty, the single-type experts may still miss it because their training datasets are limited to one lesion type, and lesions of certain appearances, sizes, or contrast phases may be uncommon in them (Fig. 3 (b)(f)). They may also
generate more FPs if their training datasets have a different distribution (patient population, contrast phase, etc.) than the target dataset (Fig. 5 (f)). Therefore, a model trained on one single dataset may struggle to achieve the best performance in practical applications. In medical diagnosis, human generalists and specialists can cooperate to combine their knowledge. We propose to synergize the dataset experts by fusing their proposals to improve the final detection recall, since it is important for radiologists not to miss critical findings. For each test image, we pool proposals from all dataset experts, then do NMS to filter the overlapped boxes. The last step is to stack the predicted 2D boxes to 3D ones if the intersection over union (IoU) of two 2D boxes in consecutive slices is greater than $\theta$. The $x$, $y$ coordinates of the final 3D box is the average of the 2D ones weighted by their detection scores.

**D. 3D False Positive Reduction (FPR)**

The FPR network is shown in Fig. 2. Its input is a 3D image patch whose center is the center of the 3D box proposal. We convert the $3 \times 3 \times 3$ Conv filters of a ResNet-18 [44] to $1 \times 3 \times 3$ in ResBlocks 1–3 and to $3 \times 3 \times 3$ in ResBlock 4 [45], which we found is better than converting all filters to $3 \times 3 \times 3$. To encode multi-scale information, we use ROI pooling to crop feature maps from 4 ResBlocks. The ROI of ResBlocks 1–3 is the 3D box and that of ResBlock4 is the whole 3D patch. Focal loss is adopted as the loss function in training. In inference, the final score of a lesion proposal is

$$s = (s_{\text{LENS}} + s_{\text{FPR}})/2,$$

i.e., the average of the detection and classification networks. FPR is helpful because it can focus on differentiating hard negative (HN) samples, namely the FPs from the detector. However, when the dataset is partially labeled, the HNs may actually be true lesions. Therefore, the missing annotations and uncertain lesions need to be removed from the FPs.

**V. MISSING ANNOTATION MINING IN PARTIALLY-LAbeLED DATASET**

In this section, we introduce three strategies to mine missing annotations (MAs) and uncertain lesions in DeepLesion, as illustrated in Fig. 4. The ideas can be generalizable to other partially-labeled lesion datasets.

**A. Cross-Slice Box Propagation**

In oncological practice, radiologists generally measure a 3D lesion on a 2D slice where it has the largest cross-sectional size according to the response evaluation criteria in solid tumours (RECIST) [11], so the DeepLesion dataset only contains 2D boxes. We can find MAs by recovering the lesion’s boxes in other slices [36], see Fig. 4 (a). We collect all 2D proposals on the training set of DeepLesion, and then group boxes in adjacent slices if their IoU is larger than $\theta$. The grouped boxes...
are called “tracklets” [34]. Next, we check the “key-slice IoU” of a tracklet, namely, if any 2D box in the tracklet overlaps with an existing annotation with IoU > θ. If so, the boxes on other slices in this tracklet are considered as mined MAs.

B. Intra-Patient Lesion Matching

Cross-slice box propagation leverages the spatial continuity of lesions, while intra-patient lesion matching utilizes their temporal continuity. In clinical practice, each patient generally undergo multiple CT scans (studies) at different time points to monitor their disease progress [9], [11]. We find that within each patient, the same lesion may be annotated in one study but not another [10]. Therefore, we can establish correspondence between detected boxes and existing annotations to recover the unannotated MAs, see Fig. 4 (b). Besides, each study typically contains multiple image volumes (series) that are scanned at the same time point but differ in reconstruction filters, contrast phases, etc. We can also mine MAs from different series similarly. We utilize the lesion embedding learned in LesaNet [40], which encodes the body part, type, and attributes of lesion images and has proved its efficacy in content-based lesion retrieval. The distance of two embeddings should be small if they are from the same lesion instance. Hence, within each patient, we compute the L2 distance in the embedding space between every annotation and every tracklet and keep those pairs whose distance is smaller than a threshold δ. Fig. 4 (c) illustrates two pairs of matched lesions. Note that the matched MAs have similar but not identical appearance with existing annotations, since they are different in time point, contrast phase, etc. Therefore, the matched MAs can still provide useful new information when they are added in training.

C. Cross-Dataset Lesion Mining

The two strategies above cannot find an MA if it does not match with any existing annotation. Our solution is to explore the semantic overlap between datasets and distill knowledge from the single-type datasets. Recall that LENS is an ensemble of multiple dataset experts and can output several groups of proposals. Our intuition is that the single-type proposals generally have higher recall and fewer FPs in their specialties compared to the DeepLesion expert. This has been discussed in Sec. IV-C and Fig. 3. Therefore, for each 2D proposal from the single-type experts, if its detection score is higher than a threshold σ and it does not overlap with existing or mined annotations, we regard the proposal as a suspicious or uncertain lesion. Then, we ignore them (exclude them in the loss function) during the retraining of LENS, see Fig. 4 (d).

Previous ULD algorithms [23–25] were all limited to the 22K labeled training slices in DeepLesion. It will bias the algorithms toward lesion-rich body parts and cause many FPs in under-represented body parts. With the three mining strategies in this section, we can mine MAs and uncertain lesions from the massive unlabeled slices to incorporate them in training and improve performance on the whole body.

VI. EXPERIMENTS

A. Data

DeepLesion [9] is a large universal lesion dataset containing 32,735 lesions annotated on 10,594 studies of 4,427 patients. It was mined from the National Institutes of Health Clinical Center based on radiologists’ routine marks to measure significant image findings [11]. Thus, it closely reflects clinical needs. The LUNA (LUng Nodule Analysis) dataset [14] consists of 1,186 lung nodules annotated in 888 CT scans. LiTS (LiVe Tumor Segmentation Benchmark) [27] includes 201 CT scans with 0 to 75 liver tumors annotated per scan. We used 131 scans of them with released annotations. NIH-Lymph Node (NIH-LN) [26] contains 388 mediastinal LNs on 90 CT scans and 595 abdominal LNs on 86 scans. Without loss of generality, we chose these three single-type datasets for joint learning with DeepLesion in this paper.

For DeepLesion, we used the official training set for training. The official test set includes only 2D slices and contains missing annotations, which will bias the accuracy. We invited a board-certified radiologist to further comprehensively annotate 1000 sub-volumes in the test set of DeepLesion using 3D bounding boxes. 200 of them were used for validation and 800 for testing. In this fully-annotated test set, there are 4,155 lesions in 34,114 slices. For LUNA, LiTS, and NIH-LN, we randomly used 80% of each dataset for training and 20% for validation. We tried to build a unified lesion detection framework and adopted the same image preprocessing and data augmentation steps [25] for all datasets. First, we normalized the image orientations of all datasets. Then, we rescaled the 12-bit CT intensity range to floating-point numbers in [0, 255] using a single windowing (-1024–3071 HU) that covers the intensity ranges of the lung, soft tissue, and bone. Every axial slice was resized so that each pixel corresponds to 0.8mm. We interpolated in the z-axis to make the slice intervals of all volumes to be 2mm. The black borders in images were clipped for computation efficiency. When training, we did data augmentation by randomly resizing each slice with a ratio of 0.8–1.2 and randomly shifting the image and annotation by -8~8 pixels in x and y axes.

B. Implementation

LENS was implemented in PyTorch based on the maskrcnn-benchmark project [47]. The backbone of LENS were initialized with an ImageNet pretrained model. We used rectified Adam (RAdam) [48] to train LENS for 8 epochs and set the base learning rate to 0.0001, then reduced it to 1/10 after the 4th and 6th epochs. It took LENS 54ms to process a slice during inference on a Quadro RTX 6000 GPU. When training LENS, each batch had 4 images sampled from the same dataset [23], where each image consisted of 9 axial CT slices for 3D feature fusion [25]. The training data in each dataset contained positive slices (with existing annotations or mined MAs) and randomly sampled negative slices (may contain uncertain lesions). Their ratio is 2:1 in each epoch. Since the datasets have different sizes, we tried to reweight the samples in the loss function, but no improvement was observed. For MA mining, we empirically chose the IoU...
threshold as $\theta = 0.5$, the distance threshold for intra-patient lesion matching as $\delta = 0.15$, the detection score threshold for cross-dataset lesion mining as $\sigma = 0.5$.

The 3D FPR was initialized with ImageNet pretrained ResNet-18 using inflated 3D [49]. We used RAdam to train it for 6 epochs and set the base learning rate to 0.0002, then reduced it to 1/10 after the 2nd and 4th epochs. The batch size was 32. When training FPR, the positive and negative samples were the TP and FP proposals of LENS on the training set of DeepLesion. If the key-slice IoU (see Sec. V-A) of a proposal and an annotation or MA is larger than $\theta$, it is considered a TP. It is an FP if its IoU is smaller than $\theta_{FP}$ with any annotation, MA, or uncertain lesion. We used $\theta = 0.5, \theta_{FP} = 0.3$. The ratio of TP and FP is 1:2 in each epoch.

### C. Metric

The free-response receiver operating characteristic (FROC) curve is the standard metric in lesion detection [9], [14], [19]. Following the LUNA challenge [14], sensitivities at 1/8, 1/4, 1/2, 1, 2, 4, 8 FPs per sub-volume are computed to show the recall at different precision levels. The average of these are referred as average sensitivity. We noticed that sometimes the detector identified smaller parts of a large or irregular lesion with a big ground-truth box (see Fig. 5 (b) column 1 for an example). The IoU may be not high enough in such cases, but the detection may still be viewed as a TP as it can also help radiologists [22]. To this end, we utilized the intersection over the detected bounding-box area ratio (IoBB) instead of IoU in evaluation. If the 3D IoBB of a proposal and a ground-truth is larger than 0.3, it is considered as a TP.

### D. Results on DeepLesion

Table I displays our main results on DeepLesion. Note that we have made the evaluation criterion significantly more practical and accurate by using manually labeled 3D boxes on 800 sub-volumes, while all existing studies were all evaluated on the partially-labeled 2D official test set. Thus, we only compared with MULAN [25], the previous state-of-the-art method on the official test set of DeepLesion. First, we replaced the region proposal network (RPN) [28] in MULAN with our proposed anchor-free proposal network (AFP) (row (a)), which showed better accuracy. Then, we added the three single-type datasets for multi-task joint training (row (b)). The average sensitivity further was improved by 0.5%. The shared backbone and FC layers in LENS can learn better feature representation through multi-source CT datasets. The improvement is not very prominent possibly because the DeepLesion dataset is already large. Experiments in the next section show multi-dataset joint training improves accuracy on small datasets significantly. Row (b) only used the output of the DeepLesion dataset expert. In (c), we further fused the proposals of the four dataset experts. The predictions of different dataset experts are complementary (Fig. 3). Therefore, fusing them improved ULD accuracy. The missing annotations (MAs) in DeepLesion can generate incorrect training signals and harm the detection accuracy. The three MA mining strategies in Sec. [V] not only mitigated this problem, but also enabled the use of massive unlabeled images in DeepLesion for training, so the accuracy was significantly improved by 8.2% in row (d). Finally, cascading a 3D FPR classifier obtained another accuracy gain of 2.8%. Our framework is scalable and can easily incorporate more datasets with heterogeneous labels, which we will investigate in the future.

### Table I

**Results with different components of the proposed framework**

| Method          | AFP   | Multi-dataset | Proposal fusion | MAM | FPR | FP@0.125 | 0.25 | 0.5 | 1   | 2   | 4   | 8   | Average |
|-----------------|-------|---------------|-----------------|-----|-----|----------|------|-----|-----|-----|-----|-----|---------|
| MULAN (baseline)| [25]  | ✓             | ✓               | ✓   | ✓   | 11.2     | 16.3 | 24.3| 32.8| 41.6| 50.9| 60.1| 33.9    |
| (b)             | ✓     | ✓             | ✓               | ✓   | ✓   | 15.8     | 21.4 | 27.9| 35.9| 43.4| 52.0| 60.9| 36.8    |
| (c)             | ✓     | ✓             | ✓               | ✓   | ✓   | 14.3     | 21.5 | 28.2| 35.1| 44.4| 53.9| 63.4| 37.3    |
| (d)             | ✓     | ✓             | ✓               | ✓   | ✓   | 15.9     | 22.8 | 30.1| 37.7| 46.7| 56.6| 66.1| 39.4    |
| (e)             | ✓     | ✓             | ✓               | ✓   | ✓   | 21.6     | 29.9 | 37.6| 46.7| 56.7| 65.8| 75.3| 47.6    |
| (f)             | ✓     | ✓             | ✓               | ✓   | ✓   | 23.7     | 31.6 | 40.3| 50.0| 59.6| 69.5| 78.0| 50.4    |

Sensitivity (%) at different FPs per sub-volume on the manually labeled volumetric test set of DeepLesion is shown. AFP: Anchor-free proposal network; MAM: Three missing annotation mining strategies in Sec. [V]; FPR: 3D false positive reduction network.

### Table II

**Comparison of different proposal networks**

| Method          | # Stage | Average sensitivity | Inference time (ms) |
|-----------------|---------|---------------------|---------------------|
| RPN [28]        | two     | 42.5                | 62                  |
| CenterNet [41]  | two     | 45.3                | 59                  |
| FCOS [49]       | one     | 41.7                | 29                  |
| FCOS            | two     | 45.7                | 54                  |
| AFP             | two     | 47.6                | 54                  |

Table II compares the accuracy and inference time per slice of different proposal networks. The AFP in LENS (row (d) in Table I) was replaced with other parts unchanged. AFP obtained better accuracy than the other three algorithms. We also tried to use FCOS as the proposal network and remove the detection head of LENS to make it a one-stage detector. It was faster but less accurate than its two-stage counterpart, indicating the importance of the detection head.

### Table III

**Ablation study of the missing annotation mining strategies**

| Method          | Average sensitivity | # 3D GT | # 2D GT | # 2D uncertain | # Training slices |
|-----------------|---------------------|---------|---------|----------------|------------------|
| No mining       | 36.8                | 22.8K   | 22.8K   | 0              | 22.4K            |
| + Cross-slice   | 37.7                | 22.8K   | 186K    | 0              | 163K             |
| + Intra-patient | 40.7                | 34.3K   | 250K    | 0              | 192K             |
| + Cross-dataset | 44.6                | 34.3K   | 250K    | 117K           | 192K             |
| + Unlabeled     | 46.8                | 34.3K   | 250K    | 442K           | 646K             |
In Table [III] we evaluate the three MA mining strategies: cross-slice box propagation, intra-patient lesion matching, and cross-dataset lesion mining. To eliminate the influence of multiple datasets, we trained LENS on DeepLesion alone. When no mining was applied, the model learned from the original 22.8K 2D lesion ground-truths (GTs) on 22.4K slices in the training set of DeepLesion. Cross-slice box propagation can infer more 2D boxes in the adjacent slices of existing lesion GTs, which brought an accuracy gain of 0.9%. Note that we randomly sampled one positive slice for each 3D GT in every training epoch. Intra-patient lesion matching discovered 11.5K new lesion instances (# 3D GT), which further improved the accuracy by 3%. We randomly checked 100 of the new instances and found 90% are true lesions. During cross-dataset lesion mining, 117K uncertain 2D boxes were mined by the single-type dataset experts. Examples of the uncertain lesions can be found in Fig. [3] i.e. the boxes that were detected by single-type dataset experts but missed by DeepLesion. Accuracy was increased by 3.9% by ignoring these boxes during training. After applying this strategy to all 640K training slices in DeepLesion, we can sample the unlabeled images in training while ignore the uncertain area, which brought a 2.2% accuracy gain.

### Table IV
**Different Strategies to Combine Multiple Datasets**

| Method               | Avg. sensitivity | Infer. time | Model size |
|----------------------|------------------|-------------|------------|
| Single dataset       | 36.8             | 1 ×         | 1 ×        |
| Data pooling [3]     | 39.4             | 1 ×         | 1 ×        |
| Positive data pooling| 32.8             | 1 ×         | 1 ×        |
| Separate models      | 39.6             | 4 ×         | 4 ×        |
| Proposed             | 47.6             | 1.8 ×       | 1.1 ×      |
| Ignored as GT        | 44.9             | 1.8 ×       | 1.1 ×      |
| Proposed + domain adapt. [23] | 47.1 | 1.9 × | 1.1 × |

Several strategies to combine multiple lesion datasets are compared in Table [IV]. They all used the same backbone and AFP. “Single dataset” learned from DeepLesion alone. “Data pooling” directly pooled DeepLesion and single-type datasets and treat them as one task. “Positive data pooling” only sampled positive regions from the single-type dataset to train with DeepLesion to avoid the influence of MAs of other types. We find data pooling improved upon single dataset but positive data pooling is actually worse, which may be because the positive samples from single-type datasets contain concept shift [5] relative to DeepLesion. Data pooling further added lots of negative samples from single-type datasets. Although there may be some MAs of other types, they may still be helpful for the model to learn the appearance of normal tissues from multi-source CT images, so as to reduce FPs and improve the sensitivity at low FP levels. This is also why leveraging the unlabeled slices in DeepLesion is useful. “Separate models” learned a detector for each dataset and fused their proposals in inference. It is the slowest approach with the largest model size. Its accuracy is better than single dataset but worse than our proposed framework, possibly because each separate model performed no better than the corresponding dataset expert in our joint learning model. Our proposed framework performed the best by integrating knowledge of multiple datasets through feature sharing, proposal fusion, and annotation mining. We also find that treating the mined uncertain lesions as ignored is better than regarding them as true lesions, possibly because they contain some noise and concept shift. The domain adaptation module [23] assigns dataset-specific feature attentions, but it did not improve probably because all datasets we used are CT images with small difference in the image domain.

Qualitative results are displayed in Fig. [5]. It is clear that the predictions of different dataset experts are complementary and fusing them can improve the final sensitivity. The single-type experts are able to detect difficult cases that are in their specialty, such as small lung nodules and lymph nodes (subplots (a)(b)(e)) and indistinct liver tumors (Fig. [3](d)) that may be missed by the universal expert. But lesions of certain appearances, sizes, or contrast phases can be uncommon in the single-type datasets, thus will be missed by the single-type experts even if they are in their specialties (e.g. the large or irregular lung nodules in (a)(b), axillary LN in (a), arterial-phase liver tumor in Fig. [5](f)). The universal dataset, on the other hand, contains more diverse training samples, thus can detect more lesion types (e.g. the inguinal lymphocyst in (c), and kidney lesions in (d)), as well as those missed by the single-type experts. Subplots (d)(e) illustrate possible issues in both single-dataset and multi-dataset learning. The single-type datasets may introduce some FPs (e.g. the LiTS expert in subplot (d)), which is possibly because the distribution discrepancy across datasets (patient population, contrast phase, etc.) makes similar image appearance carry different meanings in LiTS and DeepLesion. Domain adaptation may be needed to deal with this discrepancy. In subplot (e), the DeepLesion expert detected an FP, while the LUNA expert made the right decision. Ideally, we hope the model trust the LUNA expert more in this case. Simply assigning high weights to LUNA on all lung lesions is problematic because there are many lung lesions that LUNA cannot detect (subplots (a)(b)). Future work may include training a gating head to differentiate between dataset experts’ specialties.

### E. Results on Single-Type Datasets

The joint training strategy in LENS can improve accuracy on not only DeepLesion, but also the single-type datasets. Note that there are approaches to improve accuracy on the single-type datasets such as applying organ masks and training FPR classifiers, but they are beyond the scope of this paper. In this section, our aim is not to compare LENS with existing best algorithms specially designed for each single-type dataset, but to compare single-dataset learning with joint learning. We combined DeepLesion with a proportion of training volumes from all single-type datasets to train LENS. For comparison, we trained LENS with one single-type dataset each time of the same training size. Evaluation was made on the validation set (20% of each dataset). Fig. [5] shows that joint training always outperformed single dataset, especially when the number of training samples is smaller. The only exception is LUNA with 100% training data. This is because lung nodules have
Fig. 5. Exemplar detection results of our proposed framework on the test set of DeepLesion. Columns 1–4 are the proposals from the four dataset experts of LENS. Dataset expert $i$ corresponds to the $i$th output of the multi-task detection head in Fig. 2 that is trained on the $i$th dataset. Column 5 shows the fused proposals of the four dataset experts. Green, red, and yellow boxes indicate true positives (TP), false positives (FP), and false negatives (FN), respectively. Note that an FN box is a manual 3D ground-truth annotation in a 2D slice, thus may be slightly larger than the actual lesion in this slice. The detection scores are also displayed. We show boxes with scores greater than 0.1. Different intensity windows (soft tissue, lung) are used depending on the lesions to show. It can be found that the dataset experts are complementary. Best viewed in color.

Fig. 6. Comparison of single-dataset learning and multi-dataset joint training with different proportions of training data in the single-type datasets. We report the average sensitivity at $1/8$–$8$ FPVs per volume [14].

relatively distinct appearance, thus are easier to learn. Besides, LUNA has the most training data, so the superiority of joint training is smaller. Overall, the large and diverse DeepLesion dataset helps single-type datasets learn effective features and avoid overfitting. It is particularly useful in medical image analysis where training data is often limited. It also indicates that the network has the capacity to learn different lesion types in multiple datasets with one model. In LiTS, some liver tumors have clear separation with normal tissues, while others are subtle, making it a harder task than LUNA. NIH-LN is the most difficult dataset as lymph nodes exist throughout the body and are often hard to be discriminated from the surrounding vessels, muscles, and other organs.

VII. Conclusion

In this paper, we studied two key problems in annotation-efficient deep learning: learning with multiple heterogeneous datasets and learning with partial labels, for the purpose of improved universal lesion detection. We proposed lesion ensemble (LENS) to jointly learn from multiple datasets with feature sharing and proposal fusion. Strategies are designed to mine missing annotations from partially-labeled datasets by exploiting clinical prior knowledge and cross-dataset knowledge transfer. Our framework provides a powerful means to exploit multi-source, heterogeneously and imperfectly labeled data, significantly pushing forward the performance of universal lesion detection.
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