Generalizable multi-task, multi-domain deep segmentation of sparse pediatric imaging datasets via multi-scale contrastive regularization and multi-joint anatomical priors

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ABSTRACT

Clinical diagnosis of the pediatric musculoskeletal system relies on the analysis of medical imaging examinations. In the medical image processing pipeline, semantic segmentation using deep learning algorithms enables an automatic generation of patient-specific three-dimensional anatomical models which are crucial for morphological evaluation. However, the scarcity of pediatric imaging resources may result in reduced accuracy and generalization performance of individual deep segmentation models. In this study, we propose to design a novel multi-task, multi-domain learning framework in which a single segmentation network is optimized over the union of multiple datasets arising from distinct parts of the anatomy. Unlike previous approaches, we simultaneously consider multiple intensity domains and segmentation tasks to overcome the inherent scarcity of pediatric data while leveraging shared features between imaging datasets. To further improve generalization capabilities, we employ a transfer learning scheme from natural image classification, along with a multi-scale contrastive regularization aimed at promoting domain-specific clusters in the shared representations, and multi-joint anatomical priors to enforce anatomically consistent predictions. We evaluate our contributions for performing bone segmentation using three scarce and pediatric imaging datasets of the ankle, knee, and shoulder joints. Our results demonstrate that the proposed approach outperforms individual, transfer, and shared segmentation schemes in Dice metric with statistically sufficient margins. The proposed model brings new perspectives towards intelligent use of imaging resources and better management of pediatric musculoskeletal disorders.

1. Introduction

Semantic segmentation allows the identification and localization of meaningful anatomical structures in a medical image by extracting their boundaries and consequently acts as a crucial pre-processing step in the medical image analysis workflow guiding clinical decisions. For the management of pediatric musculoskeletal disorders, three-dimensional (3D) solid or surface models of muscles, bones, cartilages, and ligaments generated from imaging examinations can significantly assist clinicians in diagnosing pathologies, assessing morphological evolution over time, and optimally guiding treatment strategies (Hirschmann et al., 2019). An accurate understanding of the pediatric anatomy is especially needed as clinical verdict requires precise knowledge of the morphological deformity and associated joint dysfunction (Balassy and Hörmann, 2008). This study focuses specifically on ankle, knee and shoulder joints (Fig. 1) for which kinematic and dynamic analyses are based on patient-specific 3D bone models (Hirschmann et al., 2019). However, the process of segmenting magnetic resonance (MR) images typically relies on manual delineation which is tedious, time-consuming, and suffers from intra- and inter-observer variability (Jaramillo and Laor, 2008; Meyer and Jaramillo, 2008).

Figure 1: Pediatric Imaging Domains

- Ankle (Calcaneus, Talus, Tibia)
- Knee (Femur, Fibula, Patella, Tibia)
- Shoulder (Humerus, Scapula)

Ground truth delineations are in red (–).
Moreover, the pediatric musculoskeletal system may be more challenging to segment than its adult counterpart due to thinner structures, the ongoing bone ossification process, and the existence of higher anatomical variability between age groups (Balassy and Hörmann, 2008; Jaramillo and Laor, 2008; Meyer and Jaramillo, 2008). Developing robust and fully-automated segmentation techniques becomes therefore a necessity to reduce analysis time and increase the reliability of morphological assessment.

Deep learning approaches have demonstrated promising results for solving medical imaging-based tasks, including classification, detection, reconstruction, registration, and segmentation (Litjens et al., 2017; Lundervold and Lundervold, 2019). Specifically, convolutional neural networks (CNN) have become state-of-the-art methods in numerous medical imaging-based applications due to their ability to learn hierarchical representations of image features in a purely data-driven manner (Litjens et al., 2017; Lundervold and Lundervold, 2019). For medical image segmentation, most deep learning models are designed based on U-Net (Ronneberger et al., 2015) and its 3D counterpart VNet (Milletari et al., 2016) due to their impressive performances compared to other CNN architectures. Numerous refinements to the U-Net convolutional encoder-decoder architecture have been proposed, including models which embed encoders pre-trained on large non-medical imaging databases (e.g. ImageNet) (Rusakov et al., 2015) to leverage low-level features typically shared between different image types (Conze et al., 2020). Alternatively, one can mention attention models such as Attention U-Net (Att-U-Net) (Oktay et al., 2018b) which integrates attention gates on the long range skip connections (between encoder and decoder) to focus on salient features. Furthermore, U-Net and V-Net models have already been employed for segmenting musculoskeletal structures in MR images, including adult knee bones, muscles, and cartilages (Ambellan et al., 2019; Zhou et al., 2018), adult shoulder bones (He et al., 2019) as well as pediatric shoulder muscules (Conze et al., 2020). However, to the best of our knowledge, the literature on fully-automated pediatric bone segmentation and multi-joint learning schemes remains limited.

While the implementation and optimization of supervised CNN typically requires large amount of annotated data, the conception of imaging datasets is a slow and onerous process (Kohli et al., 2017) that is even more challenging for pediatric databases (Hirschmann et al., 2019). Hence, the inherent scarcity of pediatric imaging resources can induce limited generalization capabilities in neural networks and reduce their performance on unseen images, which in turn may restrict their integration into regular clinical applications. Several strategies have been reported to address this generalizability issue and avoid over-fitting. These include employing multi-task (Chen et al., 2019; Le et al., 2019; Murugesan et al., 2019; Song et al., 2020) or multi-domain learning (Kamnitsas et al., 2017; Karani et al., 2018; Valindria et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020), as well as incorporating regularization terms during optimization (Nosrati and Hamarneh, 2016; Ravishankar et al., 2017; Dalca et al., 2018; Oktay et al., 2018a; Myronenko, 2019; Boutillon et al., 2021a). Intuitively, multi-task and multi-domain models benefit from parameter sharing to learn more robust and generic representations than their individual counterparts (Zhou et al., 2021; Wang et al., 2021). Regularization schemes, for their part, leverage prior knowledge to prevent model over-fitting and have therefore proven to be effective in achieving more accurate and consistent outcomes for medical image segmentation (Nosrati and Hamarneh, 2016). Regularization constraints can originate from different prior information such as boundaries, shape, atlas, or topology (Nosrati and Hamarneh, 2016). Since the common goal of these approaches is to reduce over-fitting, it could be beneficial to combine them, as well as to design regularization terms specific to multi-task, multi-domain learning to further improve performance and to build more generalizable models.

1.1. Multi-task and multi-domain learning

For medical image analysis, multi-task learning aims at leveraging heterogeneous forms of annotations, from global image labels (e.g. healthy versus impaired musculoskeletal joint) to finer-grained and pixel-level segmentation, to improve the performance of deep models (Le et al., 2019). An additional advantage of these approaches is that a variety of tasks (e.g. classification, detection, regression, segmentation, etc.) can be solved simultaneously to provide a more complete clinical diagnosis (Song et al., 2020). Certain frameworks have also proposed to incorporate supplementary sub-tasks (e.g. contour prediction or distance map estimation) to refine coarse, non-smooth, and discontinuous segmentation predictions from convolutional models (Murugesan et al., 2019). Additionally, (Chen et al., 2019) designed an attention based reconstruction task to leverage unlabeled medical images in a semi-supervised segmentation framework. Hence, two types of multi-task strategies emerge in the literature: cascade of task-specific sub-networks (Song et al., 2020), or networks with shared encoder and task-specific decoders (Chen et al., 2019; Le et al., 2019; Murugesan et al., 2019). The former is characterized by sub-models dedicated for each task that can leverage the output of the previous network as an input, while the latter defines models with partial parameters sharing between tasks. Both approaches have been reported to perform better than traditional independent models by enabling a better cooperation between tasks (Chen et al., 2019; Le et al., 2019; Murugesan et al., 2019; Song et al., 2020). However, the developed pipelines remain specific to a given intensity domain.

In parallel, recent contributions have proposed to train models over multiple intensity domains (e.g. multi-modal, multi-scanner, multi-center, multi-protocol, etc.) with the same segmentation task, in order to leverage a greater amount of training data (Kamnitsas et al., 2017; Karani et al., 2018; Valindria et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020). These architectures aim at benefiting from the correlation between intensity domains to learn more robust domain-invariant feature representations and prove to
be particularly useful when dealing with datasets containing a limited number of samples (Karani et al., 2018). Numerous multi-domain schemes have been implemented and reported to achieve better performance than individual approaches. In particular, one can mention models exploiting transfer learning and fine-tuning between domains (Karani et al., 2018), models integrating adversarial networks to learn domain-invariant features (Kamnitsas et al., 2017), models that share their latent space only (Valindria et al., 2018; Dou et al., 2020), and models composed of domain-specific encoders and a shared decoder (Valindria et al., 2018). Following this trend to re-use and share an increasing number of parameters, (Dou et al., 2020) developed a single encoder-decoder segmentation network using shared convolutional kernels and domain-specific internal feature normalization parameters, i.e., batch normalization. While this highly compact architecture reaches superior performance for multi-modal segmentation, their methodology is specific to a given anatomical region of interest (e.g., abdomen or cardiac) and the segmentation task involved the same organs of interest across various intensity domains.

Furthermore, multi-task, multi-domain learning frameworks have been concurrently developed for natural image analysis. In the context of semantic scene labeling, (Fourey et al., 2016) proposed to train a single network over the union of multiple datasets to address the limited amount of annotated data. In their approach, each dataset is characterized by its own task (segmentation label set) and domain (intensity distribution). Hence, this framework is more generic than traditional multi-task approaches which usually focus on multiple tasks in the same domain or, traditional multi-domain techniques which consider domains containing the same set of objects. Following this, studies on universal representations in computer vision proposed to employ a single model with agnostic kernels, as visual primitives may be shared across tasks and domains, and dataset-specific layers which enable task and domain specialization (Bilen and Vedaldi, 2017; Rebuffi et al., 2017, 2018). These approaches, based on shared representations, have been reported to perform at par or superior to traditional independent models. However, to the best of our knowledge, multi-task, multi-domain learning has rarely been applied to medical image analysis, with the exception of the work of (Moeskops et al., 2016) which demonstrated that a single neural network can segment multiple anatomies (i.e., brain, breast, and cardiac) simultaneously. Nevertheless, instead of generating pixel-wise segmentation masks, their model relied on a triplanar patches-based approach that predicted the class of a single pixel per input patch, which proved to be computationally expensive. In particular, their architecture did not comprise a decoder and associated skip connections as in UNet (Ronneberger et al., 2015), to directly provide whole image segmentation leveraging the global context. Most importantly, patch-wise training lacks the efficiency of fully convolutional training to provide dense output predictions (Long et al., 2015). Their methodology also failed to account for the difference in intensity distribution between domains by, for instance, integrating internal domain-specific feature normalization.

1.2. Improved generalizability via regularization

Even though multi-task and multi-domain models can integrate task- and domain-specific information through specialized layers, task and domain prior knowledge could be further exploited to improve the generalizability of learnt shared representations. For instance, (Dou et al., 2020) introduced a knowledge distillation regularization loss whose goal is to constrain the prediction distributions of their multimodal segmentation model to be similar across domains. Similarly, (Zhu et al., 2020) imposed a Gaussian mixture distribution on the shared latent representation of their image translation network to preserve fine structures between domains. However, such a hypothesis may be too restrictive. Indeed, in representation learning, a good representation can be characterized by the presence of natural clusters corresponding to the classes of the problem (i.e., disentangled representation) (Bengio et al., 2013). Hence, a number of self-supervised representation learning techniques focus on pulling together data points from the same class and pushing apart negative samples in embedded space using a contrastive metric (Hadsell et al., 2006; Chen et al., 2020). A recent contribution extended this idea to fully-supervised image classification setting by leveraging the label information and considering many positive anchors simultaneously (Khosla et al., 2020). Thus, the contrastive regularization maximizes the performance of the classifier by imposing intra-class cohesion and inter-class separation in latent space. In the context of semi-supervised medical image segmentation, (Hu et al., 2021) exploited unannotated data by designing a contrastive loss forcing pixels from the same class to assemble in embedded space. Unlike (Zhu et al., 2020), in these non-parametric contrastive approaches, it is not necessary to define a prior distribution (e.g., Gaussian, Poisson, etc.) for the latent variables. Hence, contrastive regularization techniques appear more generic and appropriate to impose domain-specific clusters in the shared representations of deep multi-task, multi-domain models.

In addition, regularization schemes can arise from other forms of prior information such as shape models of the targeted anatomical structures. For deep learning based medical image segmentation, incorporating shape or anatomical priors has already proven to be useful in reducing the effect of noise, low contrast, and artefacts (Ravishankar et al., 2017; Dalca et al., 2018; Oktay et al., 2018a; Myronenko, 2019; Boutillon et al., 2021a). Indeed, recent works have proposed to learn a representation of the anatomy from ground truth annotations using a deep auto-encoder. Data-driven models such as auto-encoders are suitable for learning anatomical prior information due to the constrained nature of anatomical structures. Hence, anatomical priors arising from round truth annotations usually integrate position, orientation, size, and shape information of the targeted structures. The learnt non-linear anatomical representation is then integrated in the segmentation network during optimization, by enforcing the
predicted segmentation to be close to the ground truth in anatomical space using a regularization term based on Euclidean distance (Ravishankar et al., 2017; Oktay et al., 2018a). One can also employ a shape code discriminator to guide the segmentation network towards more consistent and plausible shape delineations (Boutillon et al., 2021a). However, to the best of our knowledge, none of these studies on anatomical priors have proposed to simultaneously encode multiple anatomical regions in order to leverage position, orientation, size, and shape correlations between similar anatomical objects, such as pediatric bones across distinct musculoskeletal joints.

1.3. Contributions

In this study, we propose to implement and optimize a single segmentation network over the union of multiple pediatric imaging datasets arising from separate regions of the anatomy. Unlike previous methods that operate on individual pediatric musculoskeletal joint, our framework simultaneously learns multiple intensity domains and segmentation tasks emerging from distinct anatomical joints (Fig. 1). This approach allows to overcome the inherent scarcity of pediatric MR imaging dataset, which corresponds to a novel intensity domain and segmentation task. (b) Modifications to the segmentation network with a new design based on an Efficient encoder that leverages transfer learning from natural images classification task (Tan and Le, 2019). (c) Extension of the contrastive regularization from single-scale to multi-scale and integration of multi-joint anatomical priors to further improve generalizability. (d) Finally, we perform extensive experiments including visualization and quantitative analysis of the learnt representations through t-SNE (Maaten and Hinton, 2008) algorithm and cosine similarity metric to thoroughly assess our contributions.

2. Methodology

In this section, we first describe the proposed multi-task, multi-domain segmentation network (Section 2.1) built upon Efficient-UNet (Section 2.1.1) and domain-specific layers (Section 2.1.2). We then incorporate the multi-scale contrastive regularization (Section 2.2) along with the multi-joint anatomical priors (Section 2.3) into our model.

2.1. Multi-task, multi-domain deep segmentation

Let \( D_1, ..., D_K \) be \( K \) different datasets organized such that the \( k^{th} \) dataset \( D_k = \{ x^k_i, y^k_i \}_{i=1}^{n_k} \) contains \( n_k \) pairs of greyscale images \( x^k_i \) in intensity domain \( I_k \) and their corresponding class label images \( y^k_i \) in label space \( C_k \). Each intensity domain \( I_1, ..., I_K \) is characterized by its own intensity distribution, while the label spaces \( C_1, ..., C_K \) represent separate segmentation tasks constituted of different anatomical structure of interest (plus background). Hence, the goal of multi-task, multi-domain deep segmentation is to learn a single mapping \( S \) between each intensity domain and its corresponding label space, formally \( \forall k \in [1, ..., K], \ S : I_k \rightarrow C_k \).

In what follows, the function \( S \) is approximated by a segmentation network composed of a succession of layers whose parameters must be learnt during training. More specifically, \( S : x^k_i \rightarrow S(x^k_i; \Theta, \Gamma) \) is composed of shared parameters \( \Theta \) and domain-specific weights \( \Gamma = \{ \Gamma_k \}_{k=1}^{K} \) selected based on the domain \( k \) of the input image. During training, we used the stochastic gradient descent algorithm to optimize the cross-entropy loss defined in a multi-task and multi-domain setting:

\[
L_{CE} = \frac{1}{K} \sum_{k=1}^{K} \frac{1}{n_k |C_k|} \sum_{i=1}^{n_k} \sum_{c \in C_k} y^k_{i,c} \log(\hat{y}^k_{i,c}) \tag{1}
\]

where \( \hat{y}^k_{i,c} = S(x^k_i; \Theta, \Gamma) \) was the predicted segmentation and \( |C_k| \) denoted the cardinality of the \( k^{th} \) label space. The shared parameters and domain-specific weights were simultaneously derived through this novel optimization scheme. In consequence, the network \( S \) learnt to segment all structures of interest defined in label spaces \( C_1, ..., C_K \) across all intensity domains \( I_1, ..., I_K \).
1. **Learning multi-joint anatomical priors**

2. **Multi-task, multi-domain segmentation framework**

   - **2.1.1. Efficient segmentation network with pre-trained encoder**
     
     The architecture of the neural network $S$ was based on UNet (Ronneberger et al., 2015) whose encoder branch was replaced by a classification network with weights previously trained on an image classification task (Fig. 3). Following previous work on transfer learning and fine tuning from large datasets such as ImageNet (Russakovsky et al., 2015), we assumed that leveraging a pre-trained encoder would lead to better segmentation outcomes compared to models with randomly initialized weights (Conze et al., 2020). Performance improvements have been particularly reported in low data regime (Raghu et al.) similar to our scarce pediatric dataset setting. We further advanced this strategy by integrating an Efficient classification network from the Efficient-Net family as encoder (Tan and Le, 2019). Specifically, we employed the EfficientB3 encoder which incorporates mobile inverted bottlenecks convolutional blocks (MBConv) to simultane-
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Multi-task, multi-domain segmentation network $S$ based on Efficient-UNet

Multi-joint auto-encoder

Encoder $F$[Decoder $G$

Figure 3: Proposed neural network architectures: multi-task, multi-domain segmentation network $S$ based on Efficient-UNet (top) (Ronneberger et al., 2015; Tan and Le, 2019) and multi-joint auto-encoder (bottom) comprising encoder $F$ and decoder $G$. The multi-scale embedding $(z_{s_1}, ..., z_{s_3})$ and $(z_{s_4}, ..., z_{s_9})$ are obtained via global average pooling. $[C_k]$ denotes the number of classes in the $k^{th}$ segmentation task while activations (Activ) correspond to either $\text{SiLU}$ (Efficient-UNet) or $\text{ReLU}$ (auto-encoder) functions. The multi-domain MBConv block integrates shared point-wise ($1 \times 1$) and depth-wise ($D W$) convolutions, domain-specific batch normalization (DSBN) and squeeze-and-excite (SE) modules (Tan and Le, 2019).

First, to fit the EfficientB3 image dimension, we concatenated three copies of each MR slice to extend them from single greyscale channel to three channels. The encoder branch was then built on classical convolution, batch normalization, and $\text{SiLU}$ non-linearity along with MBConv blocks (MBConv1-6, Fig. 3) consisting of point-wise and depth-wise convolutions, as well as additional squeeze-and-excite modules (Tan and Le, 2019). Specifically, combination of point-wise and depth-wise convolutions layers allows to reduce the number of parameter by leveraging the decoupling of cross-channel correlations and spatial correlations (Chollet, 2017). For their parts, squeeze-and-excite modules aim at improving performance by adaptively recalibrating channel-wise features through explicit modeling of interdependencies between channels (Hu et al., 2020). The overall architecture (i.e. depth, width, and resolution) of EfficientB3 encoder is then defined in a principled way using a compound scaling coefficient (Tan and Le, 2019). Ultimately, EfficientB3 produced a 384 dimensional output and the resulting feature-map corresponded to the central part between the contracting and expanding paths of $S$ (Fig. 3). Next, we constructed a symmetrical decoder branch with up-sampling layers, classical convolutions and MBConv blocks (Fig. 3). Contrary to encoder weights that are pre-trained on ImageNet (Russakovsky et al., 2015), the decoder weights were randomly initialized. Finally, to improve both model interpretability and performance, we employed spatial attention gates to implicitly suppress irrelevant regions of the input image while highlighting salient features (Oktay et al., 2018b). These modules attached to the skip connections selected important features using contextual information from the decoding branch (Fig. 2).

2.1.2. Domain-specific layers (DSL)

Batch normalization is a ubiquitous transformation found in deep convolutional models which aims at improving convergence speed and generalization abilities of neural networks by normalizing their internal features (Ioffe and Szegedy, 2015). However, in multi-domain learning, as the individual statistics of the intensity domains $I_1, ..., I_K$ can be very different from each other (Fig. 2), a domain-agnostic batch normalization layer could lead to defective features (Karani et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020). Specifically, if we consider the $m^{th}$ features at the $l^{th}$ layer, the mean activation over domains $K^{-1} \sum_{k=1}^{K} \mu_{l,m}^k$ could be null while the domain-specific means $\mu_{l,m}^k$ are non-zero, making a domain-agnostic normalization meaningless. Thus, to more carefully calibrate the internal features of the model, we employed domain-specific batch normalization functions (DSBN) (Karani et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020):

$$\text{DSBN}_{\rho_{l,m}^k, \sigma_{l,m}^k}(t_{i,l,m}^k) = \gamma_{l,m}^k \frac{t_{i,l,m}^k - \mu_{l,m}^k}{\sqrt{(\sigma_{l,m}^k)^2 + \epsilon}} + \beta_{l,m}^k \tag{2}$$

where $t_{i,l,m}^k$ denoted the $m^{th}$ feature-map at the $l^{th}$ layer produced by the $i^{th}$ image of the $k^{th}$ dataset, $\mu_{l,m}^k$ and $\sigma_{l,m}^k$ the domain-specific mini-batch mean and standard deviation respectively. $\epsilon = 1e-5$ was added for numerical stability. The DSBN weights $\Lambda_k = \{\rho_{l,m}^k, \beta_{l,m}^k\}$ thus comprised the domain-specific trainable shift and scale of each feature, at each layer.

Following the definition of DSBN, we modified the elementary block of convolutional models (i.e. sequence of...
convolution, batch normalization, and activation) for multi-domain learning. This novel multi-domain block was based on shared convolution, DSBN, and an activation function:

$$u_{i,l+1,m} = \rho(\text{DSBN}_{l,m} \circ k_{i,l,m} \ast \text{(\Theta} \ast * u_{i,l}^k)) \quad (3)$$

Here, $u_{i,l+1,m}^k$ was the $m$th output activations generated by the $(l + 1)$th block with the $i$th image of the $k$th dataset as input, $\rho$ was a non-linearity (e.g. ReLU, SiLU, Sigmoid, etc.), and $u_{i,l}^k$ was the output of the $i$th layer. As a convention, the input image corresponded to the input of the first layer $u_{i,0}^k = x_i^k$. As indicated in (Ioffe and Szegedy, 2015), the bias of the convolutional layer can be ignored, as its role is subsumed by the shift of the subsequent normalization transformation. Thus, the shared convolutional parameters $\Theta = \{\Theta_{l,m}\}_{l,m}$ comprised solely the convolutional filters (classical, point-wise, or depth-wise). Based on this new multi-domain block, MB-Conv modules (Tan and Le, 2019) and attention gates (Oktay et al., 2018b) (Section 2.1.1) were consequently adapted to the multi-domain setting (Fig. 3). In practice, this corresponded to the modification of each batch normalization layer into its domain-specific equivalent. For instance, as attention gates select spatial regions based on feature activations (e.g. Sigmoid activation) (Oktay et al., 2018b), we hypothesized that their multi-domain counterpart could help highlight different areas in each domain thanks to domain-specific feature calibration (Fig. 2).

As intensity domains and segmentation tasks were similar in nature (i.e. pediatric bone in MR images), we assumed that low-level features (e.g. edges, gradients, etc.) as well as high-level features (e.g. bone texture, bone shape, etc.) were similar across tasks and domains. We therefore hypothesized that shared convolutional kernels would leverage features shared among tasks and domains to be more robust than their individual counterparts, while the DSBN would enable better generalization capabilities thanks to the domain-specific feature calibration of the internal features.

Furthermore, as the $K$ segmentation tasks were distinct (Fig. 1), a domain-agnostic segmentation layer may predict classes from each label space $C_1, ..., C_K$, which is counterproductive (Fourure et al., 2016) (e.g. predicting ankle bones from a shoulder image). Hence, it was essential to employ a dedicated output layer for each domain and task pair. Specifically, if $u_{i,l}^k$ denotes the output of the penultimate layer then:

$$\hat{y}_{i,l}^k = \text{softmax}(W_k \ast u_{i,l}^k + b_k) \quad (4)$$

was a domain-specific segmentation layer which produced a segmentation mask $\hat{y}_{i,l}^k$ with $|C_k|$ classes (Fig. 3). Here, the weights of the domain-specific output segmentation layer $\Xi_k = \{W_k, b_k\}$ corresponded to the final 1x1 (i.e. point-wise) convolutional filter and associated bias.

To recapitulate, the domain-specific layers (DSL) $\Gamma_k = \{\Lambda_k, \Xi_k\}$ comprised the DSBN weights $\Lambda_k$ and the weights $\Xi_k$ of the domain-specific output segmentation layers, whereas the shared parameters $\Theta$ corresponded to the classical, point-wise, and depth-wise convolutional filters. Most notably, the domain-specific weights represented a minimal supplementary parameterization with regards to the total number of shared convolutional kernels.

### 2.2. Multi-scale contrastive regularization

Each multi-domain block (Eq. 3) mapped its input to a shared representation in which features were shifted and scaled according to their domain before applying a non-linear activation. Here, we hypothesized that learning shared representations with domain-specific clusters would enhance the generalization capabilities of the model and improve the accuracy of the segmentation predictions. More precisely, we assumed that a local variation in the output of each multi-domain block should preserve the category of the domain (Bengio et al., 2013). Hence, we designed a novel regularization term aimed at disentangling domain representations by conserving intra-domain cohesion and inter-domain separation in the shared latent space (Fig. 2). The proposed contrastive regularization was adapted from image classification (Khosla et al., 2020) to multi-task, multi-domain segmentation using the known domains labels.

However, rather than applying the contrastive regularization after each multi-domain block (i.e. after each non-linearity), we imposed the clusterization constraints at each scale of the model to reduce computational complexity. To this end, we considered an ensemble of layers indices $S$ corresponding to the different spatial scale of the segmentation network, which were symmetrically distributed between the encoder and the decoder (Fig. 3). Hence, unlike the previously proposed single-scale contrastive loss that only regularized the bottleneck activations (Boutillon et al., 2021b), our multi-scale approach untangled the domain representations at each stage of the encoder and decoder modules in a deeply-supervised manner. Since the semantic information extracted and captured by the neural network differed at each scale as well as across scales, we hypothesized that it was necessary to enforce a multi-scale regularization to achieve better generalization capabilities compared to the single scale constraint.

Let $z_{i,s} = \text{GlobalAveragePooling}(u_{i,s}^k)$ be the embedding of $x_i^k$ at scale $s \in S$ to which we applied $\text{GlobalAveragePooling}$ to project the data in a lower-dimensional space $\mathbb{R}^d$ invariant to spatial transformations (e.g. rotation, translation, flipping), allowing global comparison of image representations originating from different domains (Fig. 3). The dimensionality $d$ of the representations were thus distinct at each scale and $z_{i,s}^k$ was then normalized to lie on the unit hyper-sphere, which enabled to measure distances by using an inner product (Khosla et al., 2020).

We note $P_i^k = \{j \in [1, ..., n_k] : j \neq i\}$ the set of indexes of all images from the same domain as $x_i^k$ (i.e. positive pairs) and $n = \sum_{k=1}^{K} n_k$ the total number of images across domains.
The multi-scale contrastive loss was defined as follows:

$$\mathcal{L}_{\text{MSC}} = -\frac{1}{|\mathcal{S}|} \sum_{s \in \mathcal{S}} \sum_{1 \leq k \leq K} \frac{1}{|P_k|} \sum_{j \in P_k} \log \left( \frac{\exp(z^k_{s,j} \cdot z^k_{s,j}/\tau)}{\sum_{(k',j')} \exp(z^k_{s,j} \cdot z^{k'}_{s,j'}/\tau)} \right)$$

where $z^k_{s,j} \cdot z^k_{s,j'}$ denoted the inner product between two $L^2$ normalized representations (i.e., cosine similarity) and $\tau$ was the temperature hyper-parameter which controlled the smoothness of the loss as well as imposed hard negative/positive predictions (Chen et al., 2020; Khosla et al., 2020). As the cosine similarity was bounded in the interval $[-1, 1]$ regardless of the dimensionality of the representations, we assumed that the temperature $\tau$ should be constant over scales. Optimization of $\mathcal{L}_{\text{MSC}}$ encouraged the model to produce, at each scale, closely aligned representations for all pairs from the same domain and orthogonal representations for negative couples. Thus, the multi-scale contrastive regularization gathered the embedding from the same domain, while simultaneously separating clusters from different domains (Fig. 2).

### 2.3. Multi-joint anatomical priors

Although incorporation of the multi-scale contrastive loss improved the generalization capabilities of the model by imposing clustering in its internal representations, a supplementary constraint on output predictions could further increase performance. In this direction, recent works have proposed to integrate into the segmentation network a shape representation of the anatomy, which is learnt from ground truth segmentation masks by a deep auto-encoder (Ravishankar et al., 2017; Dalca et al., 2018; Oktay et al., 2018a). An auto-encoder is a neural network composed of an encoder $F$ which maps its input to a low-dimensional feature space that compactly encodes the characteristics of the anatomy and a decoder $G$ which reconstructs the original input from the compact representation (Fig. 3) (Ravishankar et al., 2017; Dalca et al., 2018; Oktay et al., 2018a).

We extended the standard anatomical priors framework to the multi-task, multi-domain setting by designing a multi-joint auto-encoder $AE_s : y^k_i \rightarrow G(F(y^k_i; \Theta_F, \Gamma_F); \Theta_G, \Gamma_G)$ which simultaneously learns the anatomical representation of multiple joints (Fig. 2). The weights $\Theta_F$ and $\Theta_G$ corresponded to the shared convolutional kernels of $F$ and $G$, whereas $\Gamma_F$ and $\Gamma_G$ comprised the weights of the DSBN and domain-specific input and output segmentation layers of $F$ and $G$ respectively (Fig. 3). Similar to the design of the segmentation network, the multi-joint auto-encoder integrated DSBN functions to efficiently normalize its internal feature distributions, while the input and output convolutional filters operated on the distinct anatomical structures of interest.

As all segmentation tasks solely comprised pediatric bones, we assumed that our multi-joint learning scheme would leverage anatomical features common between musculoskeletal joints to obtain a more robust representations of the anatomy.

The multi-joint auto-encoder training procedure was based on the cross-entropy loss function which penalizes the reconstruction of each joint to be dissimilar from the original input (Ravishankar et al., 2017; Oktay et al., 2018a). Moreover, based on our multi-scale contrastive regularization, we imposed a clustering constraint on the shared anatomical representations ($z^k_{s,1}, ..., z^k_{s,n}$ as denoted in Fig. 3) of the auto-encoder, to promote separated low-dimensional manifold for each anatomical joint. Hence, the loss of the auto-encoder becomes:

$$\mathcal{L}_{\text{AE}} = \mathcal{L}_{\text{CE}} + \lambda_1 \mathcal{L}_{\text{MSC}}$$

with empirically set weighting factor $\lambda_1$.

After training the multi-joint auto-encoder, we integrated its encoder component $F$ into the segmentation framework by computing a multi-joint anatomical priors term (Fig. 2). To this end, both predictions and ground truth labels of each joint were projected onto the multi-joint latent anatomical space by $F$ with learnt weights $\Theta_F$ and $\Gamma_F$. The multi-joint anatomical priors loss computed the Euclidean distance between both latent anatomical representations (Oktay et al., 2018a), as follows:

$$\mathcal{L}_{\text{MDAP}} = \frac{1}{K} \sum_{k=1}^{K} \frac{1}{n_k} \sum_{i=1}^{n_k} \left\| F(y^k_i; \Theta_F, \Gamma_F) - F(y^k_i; \Theta_F, \Gamma_F) \right\|^2$$

Minimization of this loss enforced the predicted segmentation of each joint to be in the same low-dimensional manifold as the corresponding ground truth mask (Oktay et al., 2018a) and thus encouraged anatomically consistent delineations (Fig. 2). More precisely, minimizing the Euclidean distance led to similar anatomical codes for each pair of segmentation masks. It should be emphasized that anatomical codes were represented as 2D feature maps (i.e. auto-encoder bottleneck, Fig. 3) with each value encoding a distinct feature of the anatomy. As the weights of the anatomical encoder remained fixed during this step, the two feature maps were in correspondence, with each value encoding the same global anatomical feature for both ground truth and predicted segmentation masks. Anatomical features typically encompass position, orientation, size, and shape information of each structure of interest as well as their respective intra- and inter-structure correlations. However, due to the black-box nature of deep learning models, the interpretability of each anatomical feature remained limited in practice.

The segmentation network $S$ was ultimately trained using the proposed loss function based on a combination of cross-entropy, multi-scale contrastive regularization and multi-joint anatomical priors losses:

$$\mathcal{L} = \mathcal{L}_{\text{CE}} + \lambda_2 \mathcal{L}_{\text{MSC}} + \lambda_3 \mathcal{L}_{\text{MDAP}}$$

where $\lambda_2$ and $\lambda_3$ were empirically set weighting factors.

### 3. Experiments

In this section, we explain the experiments conducted with the proposed multi-task, multi-domain network on the
pediatric musculoskeletal datasets. We first present the ankle, knee and shoulder joint MR imaging datasets (Section 3.1) followed by the compared segmentation strategies (Section 3.2). We describe the implementation details (Section 3.3) as well as the conducted predicted segmentation assessment (Section 3.4).

3.1. Imaging datasets

Experiments were performed on pediatric MR imaging datasets of three musculoskeletal joints: ankle, knee, and shoulder. Ankle and shoulder imaging datasets were acquired at Centre Hospitalier Régional Universitaire (CHRU) La Cavale Blanche, Brest, France, using a 3.0T Achieva scanner (Philips Healthcare, Best, Netherlands) while knee imaging datasets were obtained retrospectively from the Children’s Mercy Hospital, Kansas City, United States. The knee data was acquired using a 3.0T MRI scanner (MAGNETOM Skyra, Siemens Healthineers, Siemens AG). MRI data acquisition was performed in line with the principles of the Declaration of Helsinki. Ethical approvals were respectively granted by the Ethics Committee (Comité Protection de Personnes Ouest VI) of CHRU Brest (2015-A01409-40) and by the research ethics committee of the Children’s Mercy Hospital, Kansas City, United States.

Ankle joint dataset. The ankle joint dataset contained 20 MR examinations ($A_1, ..., A_{20}$) acquired on pediatric individuals aged from 7 to 13 years (average age: $10.1 \pm 2.1$ years). We included three additional pediatric ankle examinations compared to our previous study (Boutillon et al., 2021b). A T1-weighted gradient echo sequence was employed during image acquisition (TR: $7.9$ ms, TE: $2.8$ ms, FOV: $140 \times 161$ mm$^2$), with resolutions varying from $0.25 \times 0.25\times 0.50$ mm$^3$ to $0.28 \times 0.28 \times 0.80$ mm$^3$. All images were annotated by a medically trained expert (15 years of experience) to get ground truth delineations of calcaneus, talus and tibia (distal) bones, with specific label for each bone using the ITK-SNAP software (http://www.itksnap.org/).

Knee joint dataset. The knee imaging dataset consisted of 17 MR examinations ($K_1, ..., K_{17}$) extracted from a pediatric cohort composed of patients aged from 13 to 18 years old (average age: $15.4 \pm 1.6$ years). Images were acquired using a 3D Gradient Recall Echo (GRE) sequence (TR: $13.0$ ms, TE: $4.4$ ms, FOV: $320 \times 320$ mm$^2$), with resolutions ranging from $0.47 \times 0.47 \times 0.5$ mm$^3$ to $0.625 \times 0.625 \times 0.63$ mm$^3$. Segmentation masks of the femur (distal), fibula (proximal), patella and tibia (proximal) bones were manually derived using ITK-SNAP.

Shoulder joint dataset. MR images of 15 shoulder joints ($S_1, ..., S_{15}$) were obtained from pediatric individuals aged from 5 to 17 years old (average age: $11.6 \pm 4.4$ years). Images were acquired using an eTHRIVE (enhanced T1-weighted High-Resolution Isotropic Volume Examination) sequence (TR: $8.4$ ms, TE: $4.2$ ms, FOV: $260 \times 210$ mm$^2$). Image resolution varied across subjects from $0.24 \times 0.24 \times 0.60$ mm$^3$ to $0.37 \times 0.37 \times 1.00$ mm$^3$. Ground truth delineations of the humerus and scapula bones were produced following the same protocol as for ankle and knee datasets.

For each dataset, all 2D slices were downsampled to $256 \times 256$ pixels and intensities were normalized to have zero-mean and unit variance.

3.2. Experimental setups

3.2.1. Multi-task, multi-domain strategies

As a first experiment, we investigated various multi-task, multi-domain segmentation strategies with Att-UNet (Oktay et al., 2018b) as backbone architecture to assess which one would provide the best segmentation results. The compared methods built upon Att-UNet comprised four approaches (Fig. 4): individual (trained on individual domains), transfer (pre-trained on one domain and fine-tuned on the others), shared (trained on all domains at once, with all parameters shared between domains) and DSL (trained on all domains at once, with shared and domain-specific parameters). The shared approach differed from the DSL scheme by its domain-agnostic batch normalization and shared segmentation layer which predicted bones of interest from all domains with distinct labels (plus background). In this sense, the shared approach was analogous to that developed by (Moeskops et al., 2016), although their network architecture differed from Att-UNet and lacked the efficiency to provide dense segmentation predictions. In addition, all networks were trained from scratch with randomly distributed weights except in the transfer scheme in which weights learnt on one domain were transferred to other domains for initialization (Fig. 4). In the transfer scheme, models were not tested on their domain of origin because retraining on the same dataset would not have corresponded to a transfer of knowledge between domains. Hence, transfer$_{Ankle}$ denoted models pre-trained on ankle images and fine-tuned on either knee or shoulder domains. We investigated all possible combinations of transfer learning between the three datasets, and defined transfer$_{Knee}$ and transfer$_{Shoulder}$ schemes in a similar manner.

Furthermore, to evaluate the contributions of the multi-scale contrastive regularization and multi-joint anatomical priors, we performed an ablation study by setting the hyper-parameters weighting factors $\lambda_1$, $\lambda_2$, and $\lambda_3$ to zero respectively. Specifically, as the intensity domains $I_1, ..., I_K$ were not differentiated in the shared approach, the multi-scale contrastive regularization $L_{MSC}$ could only be integrated in the DSL scheme. Meanwhile, the multi-joint anatomical priors $L_{MJP}$ were incorporated in both shared (using a multi-joint auto-encoder with all parameters shared) and DSL (using a multi-joint auto-encoder with shared and domain-specific parameters) approaches. Finally, we assessed the advantages of the multi-scale contrastive over the previously proposed single-scale contrastive ($L_{SSC}$) method (Boutillon et al., 2021b) which only constrain the network bottleneck (i.e. encoder output).
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![Figure 4: Proposed multi-task, multi-domain segmentation strategies: (a) individual strategy constituted of domain-specific networks, (b) transfer strategy in which weights learnt on one domain were transferred to other domains for initialization, (c) shared strategy comprising a single network with all parameters shared between domains, and (d) domain-specific layers (DSL) strategy based on a model with shared convolutional filters along with domain-specific batch normalization and segmentation layers. The transfer strategy encompassed all possible combinations of transfer learning between the three domains including transfer\textsubscript{Ankle} (as depicted here), transfer\textsubscript{Knee}, and transfer\textsubscript{Shoulder} (both omitted for brevity).]"
training data. Data augmentation comprised random rotation (±22.5°), shifting (±10%), and flipping in both directions to teach the networks the desired invariance, covariance and robustness properties. Furthermore, the same post-processing was employed after each method: first, the obtained 2D segmentation masks were stacked together to form a 3D volume, then we selected the largest connected set of each anatomical structure as final 3D predicted mask, and we finally applied morphological closing (5×5×5 spherical kernel) to smooth the resulting boundaries.

### 3.4. Assessment of predicted segmentation

Assessment of the 3D delineations generated by the different methods relied on a comparison against manually annotated ground truths. For each dataset, Dice coefficient, sensitivity, specificity, maximum symmetric surface distance (MSSD) (i.e. symmetric Hausdorff distance), average symmetric surface distance (ASSD), and relative absolute volume difference (RAVD) metrics were computed for each bone and the average score was reported in Tables 2 and 3. Dice coefficient assesses the similarity between the two voxel sets while sensitivity and specificity measure the true positive and true negative rates respectively. Surface distances (MSSD and ASSD) determine the models’ ability to generate the same 3D contours as those produced manually. Finally, RAVD computes the volumetric difference between volumes. Moreover, an expert visually validated the global anatomical consistency and plausibility of each predicted segmentation. Please refer to the supplementary material for mathematical definition of the employed metrics.

Due to the scarce amount of pediatric examinations, experiments were performed in a leave-one-out manner such that, for each dataset, one examination was retained for validation, one for test, and the remaining data were used to train the model. We iterated through the datasets simultaneously to compute the mean and standard deviation of each metric, and used each examination at maximum once for test. We did not test all combinations between datasets, as this would have introduced redundant observations in the results and drastically increased computation time (i.e. 20 × 17 × 15 = 5100 possible combinations). Consequently, as the shoulder joint dataset contained the fewest number of MR image volumes, 5 ankle and 2 knee joint examinations were never included in the test sets since all 15 shoulder samples were already tested. Specifically, the imaging dataset with the fewest samples defined the total number of steps in the leave-one-out evaluation, as we refrained from testing examinations from this dataset multiple times to avoid redundant results and associated bias. All experiments followed the same protocol and imaging examinations with the same index (i.e. A₁, Kᵢ, and Sᵢ) indicated 3D samples tested in the same łoży fold of the leave-one-out evaluation. Following standard machine learning practice, the hyper-parameters values (r, λ₁, λ₂, λ₃, batch size, epochs, learning rate, etc.) were selected based on the performance of the model on the validation set (Table 1).

The limited amount of 3D examinations also forced us to perform the statistical analysis between methods on the 2D MR images. To compare the multi-task, multi-domain strategies, we concatenated the 2D scores obtained on each dataset to create a unique distribution per metric. Specifically, we employed the Kolmogorov-Smirnov non-parametric test using Dice, sensitivity, and specificity scores obtained from the 2649 ankle, 3041 knee, and 3682 shoulder 2D slices which corresponded to the 45 MR image volumes in the test sets. Nevertheless, to avoid distorting the scores distributions, we retained only the scores obtained from the 1294 ankle, 2283 knee, and 3357 shoulder 2D images with at least one anatomical structure of interest. The non-normality of the 2D results distributions was preliminary verified using D’Agostino and Pearson normality test. Moreover, due to the skew of the non-normal distributions, we reported their mean and the distances from the mean to the upper and lower bound of the 68% confidence interval, which correspond to the 16 and 84 percentiles, as in (Schnider et al., 2020). Since transfer models (transfer_Ankle, transfer_Knee, and transfer_Shoulder) were not tested on their original domain, we used the 2D scores obtained in the individual scheme as substitute. For each backbone architecture (Att-UNet, Inception-UNet, Dense-UNet, and Efficient-UNet) we evaluated the statistical significance of the performance obtained by our methodology based on DSL with multi-scale contrastive regularization and multi-joint anatomical priors (DSL + LMSC + L_MIAP) compared to other multi-task, multi-domain strategies and reported the results in Table 4.

Finally, we performed visual comparison of predicted...
segmentation masks at two levels. First, we evaluated the benefits in segmentation quality of the proposed multi-scale contrastive regularization ($\mathcal{L}_{\text{MSC}}$) along with multi-joint anatomical priors ($\mathcal{L}_{\text{MJAP}}$) using Att-UNet as backbone architecture in shared and DSL schemes. Second, we compared the segmentation obtained by the proposed Efficient-UNet pre-trained architecture in individual, shared + $\mathcal{L}_{\text{MJAP}}$, and DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ optimization schemes. We also provide attention maps computed by multi-domain attention gates to assess the interpretability of the proposed multi-task, multi-domain deep learning architectures (Att-UNet, Inception-UNet, Dense-UNet, and Efficient-UNet in DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ learning scheme). Specifically, we visualized the attention maps extracted by the spatial attention gate with highest resolution, which were up-sampled to original image resolution (i.e. 256 x 256) for Inception-UNet, Dense-UNet, and Efficient-UNet models.

3.5. Assessment of learnt shared representations

To assess the benefits of the proposed multi-scale contrastive regularization on the internal features of multi-domain neural networks, we compared the shared representations learnt by Att-UNet and the multi-joint auto-encoder in shared, DSL, and DSL + $\mathcal{L}_{\text{MSC}}$ schemes. First, we computed the multi-scale embeddings $z_1, ..., z_n$ of Att-UNet (respectively $\tilde{z}_{A1}, ..., \tilde{z}_{A0}$ of the multi-joint auto-encoder, Fig. 3) using ankle, knee, and shoulder 2D MR images (respectively 2D segmentation masks) originating from the training and validation sets. The 2D segmentation masks consisting of solely background were discarded during the process. Then, we applied the dimensionality reduction procedure recommended in (Maaten and Hinton, 2008), to visualize the high dimensional feature vectors belonging to $\mathbb{R}^d$ with $d$ ranging from 32 to 512 (Fig. 3). For vector space dimension $d > 50$, we first employed principal component analysis to reduce the representations to 50 dimensional feature vectors. We ultimately used the t-SNE algorithm with perplexity and learning rate respectively set to 30 and 200, to embed the data into a 2D space.

Finally, to provide a quantitative validation of the multi-scale contrastive regularization, we computed and compared the mean inter- and intra-domain cosine similarity of Att-UNet representations learnt in shared, DSL+$\mathcal{L}_{\text{SSC}}$, and DSL+$\mathcal{L}_{\text{MSC}}$ schemes. As evaluating the similarity measure of each possible data points pairs was computationally expensive, we randomly selected $10^3$ pairs within and between each domain, and reported their respective mean cosine similarity and standard deviation in Table 5.

4. Results

The proposed method based on Efficient-UNet with pre-trained encoder, DSL, multi-scale contrastive regularization, and multi-joint anatomical priors was evaluated on three pediatric imaging domains and segmentation tasks. In this section, we report the quantitative results (Section 4.1) and qualitative comparisons (Section 4.2) of the multi-task, multi-domain strategies with different backbone architectures.

4.1. Quantitative assessment

Assessment of the multi-task, multi-domain segmentation strategies using Att-UNet architecture as backbone demonstrated that the segmentation method based on DSL with multi-scale contrastive regularization $\mathcal{L}_{\text{MSC}}$ and multi-joint anatomical priors $\mathcal{L}_{\text{MJAP}}$ achieved the best results on all metrics, except for sensitivity (0.7% lower than the best) and RAVD (0.4% higher than the best) on the knee dataset (Table 2). For ankle examinations, the method outperformed other approaches in Dice (+0.3%), MSSD (−0.7 mm), ASSD (−0.1 mm) and RAVD (−0.8%), while reaching sensitivity performance (90.7%) comparable to DSL + $\mathcal{L}_{\text{MSC}}$ strategy. With respect to the scores obtained for knee bone segmentation, our approach improved MSSD (−2.3 mm) and ASSD (−0.2 mm), while achieving same Dice results (94.3%) as DSL + $\mathcal{L}_{\text{MSC}}$ scheme. Additionally, for the shoulder dataset, our method outperformed other approaches in Dice (+1.6%), sensitivity (+2.4%), MSSD (−6.4 mm), ASSD (−0.6 mm), and RAVD (−0.2%). All methods achieved excellent specificity scores on all datasets (> 99.8%, Table 2). Moreover, the statistical analysis performed on 2D slices using Dice, sensitivity and specificity metrics indicated that the proposed method (DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$) produced significant improvements in segmentation performance ($p$-values < 0.01, Table 4). The 2D results also confirmed the overall performance improvements produced by our approach on Dice (+2.1%) and sensitivity (+0.8%) scores.

We then evaluated the performance of the backbone architectures with an encoder pre-trained on ImageNet using individual, shared + $\mathcal{L}_{\text{MJAP}}$, and DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ learning schemes (Table 3). Results obtained with Inception-UNet, Dense-UNet, and Efficient-UNet models further illustrated the benefits of the proposed learning scheme based on DSL, multi-scale contrastive regularization $\mathcal{L}_{\text{MSC}}$, and multi-joint anatomical priors $\mathcal{L}_{\text{MJAP}}$. In Inception-UNet experiments, the DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ scheme ranked best in all metrics and in all datasets except for knee MSSD (0.8 mm higher than the best), shoulder sensitivity (0.7% lower than the best), and shoulder MSSD (0.2 mm higher than the best). Similarly, Dense-UNet backbone with DSL+$\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ approach ranked best in all metrics and in all datasets except for ankle sensitivity (1.3% lower than the best), knee sensitivity (1.2% lower than the best), and knee RAVD (0.2% higher than the best). For its part, the proposed Efficient-UNet with DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ achieved the best performance in all metrics and in all datasets except for ankle RAVD (1.0% higher than the best), shoulder sensitivity (1.6% lower than the best), and shoulder MSSD (1.3 mm higher than the best). Moreover, with respect to the 2D results, the proposed DSL+$\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ scheme consistently reached the best Dice performance while Shared + $\mathcal{L}_{\text{MJAP}}$ achieved the best sensitivity within each backbone (Table 4). The obtained $p$-values indicated that proposed DSL + $\mathcal{L}_{\text{MSC}}$ + $\mathcal{L}_{\text{MJAP}}$ produced statistically significant different results ($p$-values < 0.01), except compared with the individual scheme using the Efficient backbone on the sensitivity metric. In this particular case, the difference between the 2D
scores distributions was not statistically significant. However, as DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) produced statistically significant improvements on the remaining 2D metrics, we considered the overall improvements to be statistically significant.

Finally, when comparing the four backbone architectures (Att-UNet, Inception-UNet, Dense-UNet, and Efficient-UNet) with fixed DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) learning scheme (Tables 2 and 3), we observed that the proposed Efficient-UNet DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) reached the best performance in all metrics and in all datasets except for ankle RAVD (0.3% higher than Dense-UNet DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \)).

### 4.2. Qualitative assessment

Visual comparison of the multi-scale contrastive regularization \( \mathcal{L}_{MSC} \) and multi-joint anatomical priors \( \mathcal{L}_{MIAP} \) provided visual evidence of gradual improvements in segmentation quality for both shared and DSL Att-UNet models (Fig. 5). Anatomical priors were clearly observed to promote globally more consistent and smoother contours for all anatomical joints by forcing the model to follow the learnt non-linear multi-joint anatomical representation. More specifically, incorporation of anatomical priors allowed the segmentation of the complete talus (\( A_{14} \)), fibular (\( K_3 \)), and scapular shapes (\( S_{11} \) and \( S_{12} \)), which were previously partially detected by both shared and DSL Att-UNet models. Additionally, the contrastive regularization encouraged more precise bone extraction in all domains (\( A_{12} \), \( K_3 \), and \( S_{11} \)) through more robust shared representations with domain-specific clusters. Meanwhile, the proposed DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) approach fostered the benefits of both previous terms and generated smoother and more realistic bone delineations (\( A_{14} \), \( K_3 \), and \( S_{11} \)).

We then visually compared the pre-trained Efficient-UNet models employed in individual, shared + \( \mathcal{L}_{MIAP} \), and DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) learning strategies (Fig. 6). First, the qualitative comparison demonstrated that models with pre-trained

| Method                                | Dice \( \uparrow \) | Sens. \( \uparrow \) | Spec. \( \uparrow \) | MSSD \( \downarrow \) | ASSD \( \downarrow \) | RAVD \( \downarrow \) |
|---------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Individual                            | 88.2 ± 1.9        | 88.1 ± 5.4        | 99.9 ± 0.1        | 17.9 ± 10.8       | 1.9 ± 1.1         | 14.1 ± 4.6        |
| Transfer\(_{nee}\)                    | 89.5 ± 5.7        | 88.3 ± 6.0        | 99.9 ± 0.1        | 12.6 ± 10.2       | 1.6 ± 1.7         | 14.0 ± 10.9       |
| Transfer\(_{Shoulder}\)              | 89.3 ± 4.2        | 87.5 ± 6.5        | 99.9 ± 0.1        | 11.6 ± 5.0        | 1.3 ± 0.6         | 12.9 ± 8.6        |
| Shared                                | 88.8 ± 2.5        | 87.6 ± 6.3        | 99.9 ± 0.1        | 13.4 ± 8.1        | 1.5 ± 0.8         | 12.5 ± 7.0        |
| Shared + \( \mathcal{L}_{MIAP} \)    | 89.6 ± 1.6        | 90.6 ± 5.3        | 99.9 ± 0.1        | 11.0 ± 7.4        | 1.2 ± 0.8         | 10.9 ± 5.6        |
| DSL                                   | 90.6 ± 2.3        | 88.5 ± 4.6        | 99.9 ± 0.1        | 12.7 ± 9.2        | 1.3 ± 1.2         | 10.5 ± 4.4        |
| DSL + \( \mathcal{L}_{MIAP} \)       | 90.9 ± 1.9        | 89.1 ± 4.6        | 99.9 ± 0.1        | 9.0 ± 3.0         | 1.0 ± 0.3         | 11.3 ± 4.7        |
| DSL + \( \mathcal{L}_{SSC} \)        | 90.6 ± 2.1        | 87.7 ± 4.9        | 99.9 ± 0.1        | 9.7 ± 3.7         | 1.0 ± 0.3         | 9.6 ± 4.2         |
| DSL + \( \mathcal{L}_{MSC} \)        | 91.5 ± 2.0        | 90.7 ± 4.7        | 99.9 ± 0.1        | 9.0 ± 2.9         | 0.9 ± 0.3         | 8.8 ± 4.7         |
| DSL + \( \mathcal{L}_{MSC} + \mathcal{L}_{MIAP} \) | 91.8 ± 1.8        | 90.7 ± 4.8        | 99.9 ± 0.1        | 9.0 ± 2.9         | 0.9 ± 0.3         | 8.8 ± 4.7         |

Table 2: Leave-one-out quantitative assessment of Att-UNet (Oktay et al., 2018b) using individual, transfer, shared, and DSL strategies employed with single-scale contrastive regularization \( \mathcal{L}_{SSC} \), multi-scale contrastive regularization \( \mathcal{L}_{MSC} \), and multi-joint anatomical priors \( \mathcal{L}_{MIAP} \) on ankle, knee, and shoulder datasets. Metrics include Dice (%), sensitivity (%), specificity (%), MSSD (mm), ASSD (mm), and RAVD (%). Mean scores and standard deviations reported in bold and underlined respectively correspond to the first and second best results obtained for each dataset.
| Method        | Ankles         | Sens. | Spec. | MSSD | ASSD | RAVD |
|--------------|----------------|-------|-------|------|------|------|
| Ankle        | Individual     | 91.4  | 92.2  | 99.9 | 8.5  | 0.9  | 9.7  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 91.3  | 91.6  | 99.9 | 9.8  | 1.0  | 10.0 |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 93.2  | 92.2  | 99.9 | 6.5  | 0.7  | 7.4  |
| Knee         | Individual     | 93.9  | 92.1  | 99.9 | 5.5  | 0.5  | 6.9  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 94.2  | 93.0  | 99.9 | 6.4  | 0.5  | 6.0  |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 94.5  | 93.6  | 99.9 | 6.3  | 0.5  | 5.2  |
| Shoulder     | Individual     | 82.8  | 79.6  | 99.9 | 21.8 | 2.1  | 15.9 |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 83.1  | 81.2  | 99.9 | 20.0 | 1.7  | 16.4 |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 84.5  | 80.5  | 99.9 | 20.2 | 1.6  | 14.7 |
| Dense-UNet   | Ankle          | 93.4  | 92.8  | 99.9 | 6.9  | 0.7  | 6.6  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 93.4  | 92.5  | 99.9 | 6.4  | 0.7  | 6.6  |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 93.1  | 92.6  | 99.9 | 5.2  | 0.5  | 5.6  |
|              | Individual     | 94.3  | 92.6  | 99.9 | 4.6  | 0.5  | 4.5  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 95.1  | 94.9  | 99.9 | 4.5  | 0.5  | 4.7  |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 95.1  | 93.7  | 99.9 | 4.5  | 0.5  | 4.7  |
|              | Individual     | 82.5  | 79.5  | 99.9 | 22.1 | 1.9  | 16.2 |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 84.9  | 85.2  | 99.9 | 20.2 | 1.4  | 14.9 |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 86.4  | 87.0  | 99.9 | 16.0 | 1.2  | 11.5 |
|              | Individual     | 92.3  | 92.0  | 99.9 | 7.0  | 0.8  | 8.2  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 93.8  | 93.5  | 99.9 | 6.5  | 0.6  | 5.9  |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 93.8  | 93.5  | 99.9 | 5.6  | 0.6  | 6.9  |
|              | Individual     | 94.1  | 93.0  | 99.9 | 4.7  | 0.5  | 5.7  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 95.0  | 94.3  | 99.9 | 4.8  | 0.5  | 4.1  |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 95.4  | 95.0  | 99.9 | 4.2  | 0.4  | 3.8  |
|              | Individual     | 87.7  | 86.8  | 99.9 | 16.0 | 1.0  | 8.4  |
|              | Shared + $\mathcal{L}_{\text{MIAP}}$ | 86.9  | 89.0  | 99.9 | 14.3 | 0.9  | 10.7 |
|              | DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ | 87.9  | 87.4  | 99.9 | 15.6 | 1.0  | 7.3  |

Table 3: Leave-one-out quantitative assessment of the pre-trained architectures: Inception-UNet (Szegedy et al., 2016), Dense-UNet (Huang et al., 2017), and Efficient-UNet (Tan and Le, 2019) on ankle, knee, and shoulder datasets. Individual, shared, and DSL strategies are employed with multi-scale contrastive regularization $\mathcal{L}_{\text{SC}}$ and multi-joint anatomical priors $\mathcal{L}_{\text{MIAP}}$. Metrics include Dice (%), sensitivity (%), specificity (%), MSSD (mm), ASSD (mm), and RAVD (%). Mean scores and standard deviations reported in bold and underlined respectively correspond to the first and second best results obtained for each dataset.

encoder benefited from transfer learning to achieve robust feature extraction and produce highly accurate delineations in the three considered anatomical regions ($A_{11}$, $K_{15}$, and $S_5$). However, we observed that individual models produced segmentation errors in several imaging examinations, for instance, by over-segmenting the femoral shape in knee joint ($K_{11}$) or under-segmenting the scapular bone in shoulder joint ($S_5$). Specifically, because the boundary between bone and ligament was not detected by the individual model, ligamentous tissues were erroneously classified as femur bone ($K_{11}$). Furthermore, the thin structure of scapular bone led to its partial misclassification as background ($S_5$). Additionally, the calcaneus shape was also under-segmented due to intensity difference within the bone ($A_{11}$). While the shared + $\mathcal{L}_{\text{MIAP}}$ model produced segmentation improvements over its individual counterparts, it was essential to employ the DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ model incorporating layer specialization along with multi regularizers to learn robust shared representations and achieve precise bone shape predictions on unseen images ($A_{11}$, $K_{15}$, and $S_5$).

Finally, we provide visualization of the attention maps computed by the multi-domain attention gates of the Att-UNet, Inception-UNet, Dense-UNet, and Efficient-UNet architectures employed in DSL + $\mathcal{L}_{\text{SC}}$ + $\mathcal{L}_{\text{MIAP}}$ learning scheme (Fig. 7). These attention maps were crucial in interpreting the inference process of deep neural networks. This visualization confirmed that the segmentation models exploited the spatial and contextual information from the encoder branch to focus on the bone of interest in each anatomical joint. Indeed, knee attention maps clearly equally highlighted each bone of interest (femur, fibula, patella, and tibia), and suppressed most of the irrelevant regions. In some cases, background elements were also included (e.g. $A_9$ with Inception-UNet and $S_{12}$ with Dense-UNet) and may help the inference process which remains difficult to interpret. We can note that attention maps computed on shoulder joint images high-
lighted the scapula less than the humerus bone. Meanwhile, ankle joint attention maps focused on the calcaneus, talus, and tibia bones, with some background structures also being highlighted. Finally, for each bone of interest, we observed a discontinuity in the attention coefficients at the bone borders (e.g. $K_3$ with Efficient-UNet), that allowed the network to effectively distinguish and extract their shape from the rest of the image.

5. Discussion

In this study, we developed and evaluated a novel multi-task, multi-domain deep segmentation framework with multi-scale contrastive regularization and multi-joint anatomical priors. To the best of our knowledge, the proposed multi-task, multi-domain segmentation method is the first illustration to optimize a single neural network over multiple pediatric musculoskeletal joints. Experiments performed on the ankle, knee, and shoulder joint imaging datasets demonstrated improved bone segmentation performance compared to individual, transfer, and shared learning schemes. The statistical analysis validated the significance of the results, while visual comparison of the predicted delineations further confirmed the enhancements in segmentation quality of the proposed framework. The proposed methodology could provide significant benefits to the management of pediatric imaging resources and have a major impact for any deep learning based medical image analysis framework.

5.1. Segmentation performance

Regarding the performance of the multi-task, multi-domain strategies employed with Att-UNet architecture, we observed that all transfer learning schemes (TransferAnkle, TransferKnee, and TransferShoulder) provided performance improvements compared to individual models on all datasets (Table 2), indicating better initialization than randomly set weights by exploiting features correlation and knowledge transfer between each task and domain pair. Compared to individual and trans-
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![Image showing visual comparison of multi-scale contrastive regularization](image)

**Figure 5:** Visual comparison of the multi-scale contrastive regularization $L_{MSC}$ and multi-joint anatomical priors $L_{MJAP}$ using Att-UNet architecture. Automatic segmentation of ankle, knee, and shoulder bones based on Att-UNet (Oktay et al., 2018b) employed in shared and DSL strategies. Ground truth delineations are in red (-) while predicted bones appear in green (-) for calcaneus, blue (-) for talus, yellow (-) for tibia (distal), orange (-) for femur (distal), pink (-) for fibula (proximal), light green (-) for patella, light blue (-) for tibia (proximal), magenta (-) for humerus, and cyan (-) for scapula.

fer approaches, the results of shared and DSL schemes on both ankle and knee datasets indicated noticeable improvements while the results on shoulder examinations were less evident (Table 2). Hence, it was essential to employ both $L_{MJAP}$ and $L_{MSC}$ terms to benefit from the shared representation and layer specialization, and reach performance improvements over independent models on all datasets. This outcome was also supported by the results obtained on Inception-UNet, Dense-UNet, and Efficient-UNet models (Table 3). It is also worth emphasizing that the multi-scale contrastive $L_{MSC}$ regularization outperformed its single-scale $L_{SSC}$ counterpart (Boutillon et al., 2021b) on all datasets (Table 2), indicating that disentangling representations at each scale provided better generalization performance than focusing only on the features within the network’s bottleneck. For instance, the ankle Dice score increased from 90.6% to 91.5%, while knee and shoulder Dice metrics improved by 0.7% and 0.8% respectively.

Furthermore, both shared and DSL schemes offer an additional advantage compared to transfer approach by learn-
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Figure 6: **Visual comparison of the pre-trained Efficient-UNet models.** Automatic segmentation of ankle, knee, and shoulder bones based on Efficient-UNet (Tan and Le, 2019) employed in individual, shared + LMJAP, and DSL + LMJAP + LMSC + LMJAP strategies. Ground truth delineations are in red (–) while predicted bones appear in green (–) for calcaneus, blue (–) for talus, yellow (–) for tibia (distal), orange (–) for femur (distal), pink (–) for fibula (proximal), light green (–) for patella, light blue (–) for tibia (proximal), magenta (–) for humerus, and cyan (–) for scapula.

When comparing the performance of the four employed backbone architectures in the individual learning scheme (Tables 2 and 3), we observed that Inception-UNet, Dense-UNet, and Efficient-UNet outperformed Att-UNet in all metrics and in all datasets. As also highlighted in (Conze et al., 2020) for shoulder muscle MR segmentation, this clearly indicated that designing a segmentation model with a pre-trained encoder resulted in better initialization through features learnt on ImageNet and better segmentation performance through a more complex and deeper CNN architecture. Indeed, compared to the complexity of the Att-UNet model, the number of trainable parameters in Inception-UNet, Dense-UNet and Efficient-UNet corresponded to an increase by a factor of five, three, and two respectively (Table 1). However, to avoid overfitting it is also crucial to limit the number of trainable parameters, as models with too much capacity may learn the dataset and task too well. In practice, the optimal model capacity depends on the considered task and available imaging resources which are limited in the context of sparse pediatric datasets. In this sense, we observed step-wise performance improvements from Inception-UNet (48.3M parameters) to Dense-UNet (23.6M parameters) and ultimately Efficient-UNet (14.8M parameters) networks (Table 3). For instance, shoulder Dice score increased from 84.5% for Inception-UNet to 86.6% for Dense-UNet and ultimately to 87.9% using Efficient-UNet. Finally, the proposed multi-task, multi-domain approach also allowed us to reduce the number of learnable parameters by a factor of $K = 3$, and to consequently minimize overfitting and improve generalizability. Meanwhile, the supplementary parameterization introduced by the domain-specific layers was considered marginal (i.e. less than 3%).

As demonstrated through our experiments, the proposed DSL + LMSC + LMJAP learning scheme is architecture-independent, and thus can be effortlessly integrated into various existing CNN models and can improve the overall performance in all datasets. Indeed, although the obtained Dice and ASSD performance gains can be considered limited, these
Improvements are consistent and robust (i.e. lower standard deviation). Most importantly, experiments performed on Inception-UNet, Dense-UNet, and Efficient-UNet illustrated that the multi-scale contrastive regularization can be computed from the internal representations of networks composed of distinct building blocks (i.e. Inception, dense, or MBConv blocks) and diverse feature transformation operation (i.e. classical, point-wise, depth-wise, or asymmetrical convolutions and ReLU or SiLU non-linearity functions).

As indicated by the high variance in shoulder results (Tables 2 and 3), the shoulder dataset was more challenging to segment than the ankle and knee joints, due to more complex bone shapes (i.e. thin scapular blade), higher variability among pediatric patients (i.e. different age groups), and the presence of examinations with a higher level of noise due to patient movements during acquisition. Interestingly, the attention maps (Fig. 7) could explain the lower performance for segmenting the scapular shape which appeared more challenging to detect than the humerus bone. Finally, compared to our previous experiments performed in (Boutillon et al., 2021b), we incorporated three additional ankle pediatric examinations with a higher level of noise in the test sets which led to a marginal drop in performance for ankle bone segmentation. Nevertheless, we still observed that for the ankle joint segmentation, the DSL scheme outperformed the shared approach, which in turn outperformed the individual scheme.

5.2. Assessment of learnt shared representations

The visualization of the shared representation provided an indirect analysis of the inference process of deep neural networks and a qualitative validation of the benefits of the additional multi-scale contrastive regularization on both intra-domain cohesion and inter-domain separation (Fig. 8). In both Att-UNet and auto-encoder networks, the shared representation learnt using shared and DSL schemes did not present margins between domains. More specifically, shared models presented mixed features with most discriminative domain disentanglement in the network bottleneck ($s_5$) which corresponded to the higher dimensional vector space ($d = 512$) allowing more robust differentiation between domains. On the contrary, the addition of the contrastive regularization led to distinctive domain-specific clusters at each scale of both networks. Hence, the shared representations of our
proposed neural networks were invariant to local variations and preserved the category of the input domain through the different scales of the models. Moreover, the generalization capabilities of the networks were visually attested as validation data points were located inside their respective domain clusters.

The quantitative evaluation (Table 5) further supported the visualizations obtained through the t-SNE algorithm (Fig. 8). Indeed, the shared Att-UNet representations presented inter-domain cosine similarity measures with high mean (> 0.58) and standard deviation (> 0.06) suggesting entangled domain representations with low cohesion. Moreover, as previously mentioned, the network bottleneck corresponding to the representation \( z_{s_0} \) (Fig. 8) presented better domain disentanglement due to higher dimensionality. Additionally, the multi-scale contrastive regularization expectedly led to, at each scale, an increase in intra-domain similarity (> 0.98) indicating more closely aligned representations from the same domain and a decrease in inter-domain similarity (< 0.47) reflecting more discriminative (i.e. orthogonal) representations between different domains. However, we observed that domain representations were less disentangled at scale \( s_0 \) (inter-domain similarity greater than 0.39) than at scales \( s_1 \) and \( s_2 \) (inter-domain similarity lower than 0.34). Therefore, the effectiveness of contrastive learning to disentangle domain representations varies at each scale, as we observed a quantitative difference in the cosine similarity of the learnt representations. Finally, we also assessed the representations learnt with the single-scale contrastive regularization which only constrained the network bottleneck (i.e. encoder output or \( z_{s_0} \)) (Boutilon et al., 2021b). Compared with \( \mathcal{L}_{\text{MSC}}^{s_1} \), only the representation associated with the 5th scale was disentangled while \( z_{s_0} \) and \( z_{s_2} \) were not affected by the single-scale contrastive constraint. This further supported the necessity to employ a multi-scale contrastive \( \mathcal{L}_{\text{MSC}} \) regularization to disentangle representations at each scale.
### 5.3. Benefits for clinical practice

Current deep learning models are specific to anatomical regions of interest and may suffer from the limited availability of imaging data, which is exacerbated in pediatric clinical workflows. Our approach demonstrated that designing a collaborative framework incorporating multi-anatomy datasets with close intensity domains and related segmentation tasks can lead to performance improvements on each dataset. In turn, this could lead to more efficient utilization of imaging resources (pediatric or adult), most notably for the treatment of musculoskeletal disorders affecting different anatomical joints. Several patient cohorts impaired by distinct pathologies could be leveraged to optimize a single model with enhanced generalization capabilities, thus reducing the overall cost of medical image acquisition. More generally, our approach could be transposed to other sets of anatomical structures sharing common characteristics, such as blood vessels in brain, lungs, and retina images (Moccia et al., 2018). Additionally, the multi-scale contrastive regularization could be integrated to enhance vascular segmentation by imposing domain-specific clusters in the embedded spaces of the shared neural network.

Similar to earlier studies employing highly compact multi-domain models (Karani et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020), our work demonstrated that deep neural networks can easily learn related segmentation tasks across multiple intensity domains. Specifically, this study further confirmed the usefulness of employing DSBN functions for multi-domain learning, which were previously successfully applied for multi-modal, multi-scanner, multi-center, or multi-protocol segmentation (Karani et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020) and have now proven to be equally effective in a multi-anatomy scenario. Furthermore, when dealing with pediatric patients, it may be beneficial to define domains corresponding to different age groups, as anatomy is significantly modified during child development. However, in the current study, we were unable to explore such multi-age setting due to the limited amount of imaging resources per age group. Finally, as opposed to previous plain UNet models developed in (Karani et al., 2018; Chang et al., 2019; Dou et al., 2020; Liu et al., 2020), our model relied on a more complex architecture based on an pre-trained EfficientB3 encoder to achieve more accurate segmentation and integrated multi-domain spatial attention gates to improve its interpretability.

### 5.4. Limitations

This study has certain limitations which are categorically listed in this section. First, although the coarse localization of the anatomical structures of interest computed by attention gates and the t-SNE visualizations of the learnt shared representations provide some interpretability of the network inference process, these approaches do not fully explain the features learnt by the segmentation model. Similarly, even though incorporating regularization through the loss function successfully constrains the network parameters and promotes the desired generalizable characteristics during training, the optimization procedure of deep neural networks remains difficult to analyse. Specifically, while the constraints computed by the multi-scale contrastive regularization are explicit, the interpretability of the multi-joint anatomical priors, on its part, is limited as it is based on a deep auto-encoder. It is thus essential to develop more interpretable models allowing a finer analysis of the internal behaviour of the framework during training and inference. In this direction, (Zhang et al., 2018) have proposed an interpretable CNN which provides a clear semantic representation by assigning to each filter a specific object part to explicitly memorize during the learning process. Such interpretable model could therefore be of great interest for medical image analysis applications, as it would allow a better analysis of the network failures.

Second, while a common hypothesis in machine learning is that the training and test data originate from the same data distribution, an emerging field (i.e. domain generalization or out-of-distribution generalization) has proposed to

| Cosine similarity | \( z_s \) (\( d = 32 \)) | \( z_s \) (\( d = 512 \)) | \( z_s \) (\( d = 32 \)) |
|-------------------|----------------|----------------|----------------|
| **Ankle**         | 0.84(0.16)     | 0.82(0.20)     | 0.86(0.14)     |
| **Knee**          | 0.84(0.11)     | 0.58(0.20)     | 0.73(0.17)     |
| **Shoulder**      | 0.83(0.10)     | 0.69(0.12)     | 0.86(0.09)     |

Table 5: Quantitative analysis based on cosine similarity of the shared representations learnt by Att-UNet in shared, DSL + \( L_{SSC} \), and DSL + \( L_{MSC} \) strategies using ankle, knee, and shoulder datasets. The included scales correspond to the encoder first layer (\( s_1 \)), network bottleneck (\( s_5 \)), and decoder last layer (\( s_9 \)). Mean and standard deviation similarity measures are reported.
address the more challenging setting in which the goal is to learn a model that can generalize to an unseen test domain (Zhou et al., 2021; Wang et al., 2021). In the present study, although our model managed multiple domains, we only addressed plain generalizability within each (i.e. unseen test image from the same distribution as the training data). While the performance improvements obtained during the leave-one-out evaluation indicated better generalization abilities within each domain, our model is currently unable to generalize on new unseen domains (e.g. new modality or anatomical joint). In the context of life-long learning in which a single model continuously learns new domains, (Karani et al., 2018) has demonstrated that DSBN parameters could be fine tuned with limited amount of training data from the novel domain, while the convolutional filters remained fixed. We assumed that our model could be similarly fine tuned on a new domain without forgetting the knowledge learnt on the previous domains. However, this approach still requires access to labelled imaging data from the new domain, unlike domain generalization frameworks in which data from the new test domain is assumed to be unavailable. Out-of-distribution generalization is thus more generic than traditional domain adaption techniques or life-long learning schemes. Therefore, domain generalization appears crucial for medical image segmentation, where each anatomical region and acquisition protocol defines a new domain in which imaging resources are not necessarily available for network training or fine-tuning purposes.

5.5. Perspectives

As our experiments were conducted on only one imaging modality (i.e. T1-weighted MR), we were unable to evaluate the genericity of our approach over multiple modalities (e.g. T2-weighted MR, CT, etc.) because of the lack of available data. However, previous studies have already demonstrated that a single neural network incorporating shared convolutional filters and DSBN functions can effectively process both CT and MR modalities simultaneously (Dou et al., 2020). So, we assumed that our model could be easily extended to multiple modalities. Similarly, we limited our experiments to bone tissue segmentation without considering other musculoskeletal tissues such as muscle, ligaments, or cartilages due to the unavailability of annotations. We also hypothesised that our framework could be upgraded to multitissue segmentation since (Zhou et al., 2018; Ambellan et al., 2019; Conze et al., 2020) have already demonstrated that deep learning models can effectively segment knee cartilages, knee muscles, and shoulder muscles, respectively. More generally, whereas methods developed on natural images employed up to ten domains (Rebuffi et al., 2018), our experiments involved only three imaging domains due to the scarcity of pediatric imaging resources and the lack of open access pediatric databases. Hence, future studies are aimed at incorporating supplementary MR imaging sequences to further promote generic features during optimization and segmenting additional tissues to provide a more complete description of the musculoskeletal system. Finally, in this direction of including an increasing number of imaging datasets, it may be beneficial to adapt our framework to federated learning scenarios similar to the ones developed by (Shen et al., 2021) for multi-task pancreas segmentation. This would allow optimization of a single model using training data from multiple institutions without centralizing imaging resources, thus allowing to prevent data privacy and security issues, which is crucial in medical workflows (Shen et al., 2021).

Furthermore, we did not consider 3D architectures in our experiments due to their higher computational complexity and GPU memory consumption compared to their 2D counterparts (Milletari et al., 2016). Although our models did not integrate a third spatial dimension, we observed smooth delineations in all directions, indicating continuous segmentation predictions between adjacent 2D slices. Additionally, our experiments were performed using only four neural network architectures (Att-UNet, Inception-UNet, Dense-UNet, and Efficient-UNet), hence it would be beneficial to include supplementary comparisons based on additional deep learning models including Transformers-based ones (Hatamizadeh et al., 2022) to further evaluate the genericity of our contributions. One could also consider an ensemble approach integrating all backbone architectures to combine the advantages of each model. Finally, with respect to the contrastive learning, we assumed that the temperature hyper-parameter \( \tau \) should be constant at each scale, as the cosine similarity between representations was bounded in \([-1, 1]\) regardless of scale. However, we observed in Table 5 that contrastive learning was less efficient at certain scales. Specifically, in the DSL+\( \mathcal{L}_{\text{MSC}} \) learning scheme, the shared representation of the 9th scale was less disentangled than in 1st and 5th scales. Hence, one could also propose to employ different temperatures at each scale and to learn such parameters during training, so that the contrastive metric be more sensitive at each scale and better disentangle representation between domains. Nevertheless, such a training procedure might be more challenging to optimize due the numerical instability associated with learnable temperature parameters.

6. Conclusion

Developing generalizable deep segmentation model is fundamental to provide accurate and reliable delineations on unseen images for clinical and morphological evaluation of the pediatric musculoskeletal system. This paper introduced a multi-task, multi-domain learning framework for pediatric bone segmentation in sparse MR imaging datasets acquired on separate anatomical joints. This multi-anatomy approach simultaneously benefited from robust shared representations and specialized layers that fitted to the domain-specific intensity distributions and task-specific segmentation label sets. Furthermore, the generalization capabilities of the segmentation model were enhanced by exploiting a multi-scale contrastive regularization to enforce domain clustering in the shared representations and multi-joint anatomical priors which encouraged anatomically consistent shape predictions.
An important perspective from this study is that collaborative utilization of pediatric resources and intelligent design of deep learning models can improve the segmentation performance on small musculoskeletal imaging datasets. Nevertheless, our framework currently provides an incomplete description of the pediatric musculoskeletal system which solely encompasses bone tissues. Hence, future work is aimed at improving our model to segment other anatomical structures (e.g., ankle cartilages, knee ligaments, or shoulder muscles). Thus, morphological and functional analysis will rely on a more complete modeling of the musculoskeletal system, towards a better management of pediatric disorders.

Compliance with ethical standards

MR image acquisition on the pediatric cohorts used in this study were performed in line with the principles of the Declaration of Helsinki. Ethical approvals were respectively granted by the Ethics Committee (Comité Protection de Personnes Ouest VI) of CHRU Brest (2015-A01409-40) and by the research ethics committee of the Children’s Mercy Hospital, Kansas City, United States. Acknowledgments

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References

F. Ambellán, A. Tack, M. Ehlike, and S. Zachow. Automated segmentation of knee bone and cartilage combining statistical shape knowledge and convolutional neural networks: Data from the osteoarthritis initiative. Medical Image Analysis, 52:109–118, 2019. ISSN 1361-8423. doi: 10.1016/j.media.2018.11.009.

C. Balassy and M. Hörmann. Role of MRI in paediatric musculoskeletal conditions. European Journal of Radiology, 68(2):245–258, 2008. ISSN 0720-048X. doi: 10.1016/j.ejrad.2008.07.018.

Y. Bengio, A. Courville, and P. Vincent. Representation learning: A review and new perspectives. IEEE Transactions on Pattern Analysis and Machine Intelligence, 35(8):1798–1828, 2013. ISSN 1939-3595. doi: 10.1109/TPAMI.2013.50.

H. Bilen and A. Vedaldi. Universal representations: The missing link between faces, text, planktons, and cat breeds. arXiv:1701.07275 [cs.CV], 2017.

A. Boutillon, B. Borotikar, C. Pons, V. Burdin, and P.-H. Conze. Multi-structure deep segmentation with shape priors and latent adversarial regularization. In 2021 IEEE 18th International Symposium on Biomedical Imaging (ISBI), pages 999–1002, 2021a. doi: 10.1109/ISBI48211.2021.9434104.

A. Boutillon, P.-H. Conze, C. Pons, V. Burdin, and B. Borotikar. Multi-task, multi-domain deep segmentation with shared representations and contrastive regularization for sparse pediatric datasets. In M. de Bruijine, P. C. Cattin, S. Cotin, N. Padoy, S. Speidel, Y. Zheng, and C. Essert, editors, Medical Image Computing and Computer Assisted Intervention – MICCAI 2021, Lecture Notes in Computer Science, pages 239–249. Springer International Publishing, 2021b. ISBN 978-3-030-87193-2. doi: 10.1007/978-3-030-87193-2_23.

W.-G. Chang, T. You, S. Seo, S. Kwak, and B. Han. Domain-specific batch normalization for unsupervised domain adaptation. In 2019 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR), pages 7346–7354, 2019. doi: 10.1109/CVPR.2019.00753.

S. Chen, G. Bortsova, A. García-Uceda Juárez, G. van Tulder, and M. de Bruijine. Multi-task attention-based semi-supervised learning for medical image segmentation. In D. Shen, T. Liu, T. M. Peters, L. H. Staib, C. Essert, S. Zhou, P.-T. Yap, and A. Khan, editors, Medical Image Computing and Computer Assisted Intervention – MICCAI 2019, Lecture Notes in Computer Science, pages 457–465. Springer International Publishing, 2019. ISBN 978-3-030-32248-9. doi: 10.1007/978-3-030-32248-9_51.

T. Chen, S. Kornblith, M. Norouzi, and G. Hinton. A simple framework for contrastive learning of visual representations. In International Conference on Machine Learning, pages 1597–1607. PMLR, 2020. URL http://proceedings.mlr.press/v119/chen20j.html.

F. Chollet. Xception: Deep learning with depthwise separable convolutions. In 2017 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), pages 1800–1807, 2017. doi: 10.1109/CVPR.2017.195.

P.-H. Conze, S. Brochard, V. Burdin, F. T. Sheehan, and C. Pons. Healthy versus pathological learning transferability in shoulder muscle MRI segmentation using deep convolutional encoder-decoders. Computerized Medical Imaging and Graphics, 83:101733, 2020. ISSN 0895-6111. doi: 10.1016/j.compmedimag.2020.101733.

A. V. Dalca, J. Guttag, and M. R. Sabuncu. Anatomical priors in convolutional networks for unsupervised biomedical segmentation. In 2018 IEEE/CVF Conference on Computer Vision and Pattern Recognition, pages 9290–9299, 2018. doi: 10.1109/CVPR.2018.00968.

Q. Dou, Q. Liu, P. A. Heng, and B. Glocker. Unpaired multi-modal segmentation via knowledge distillation. IEEE Transactions on Medical Imaging, 39(7):2415–2425, 2020. ISSN 1558-254X. doi: 10.1109/TMI.2019.2963882.

D. Fourure, R. Emonet, E. Fromont, D. Muselet, A. Trémeau, and C. Wolf. Semantic segmentation via multi-task, multi-domain learning. In S+SSPR 2016 The joint IAPR International Workshops on Structural and Syntactic Pattern Recognition (SSPR 2016) and Statistical Techniques in Pattern Recognition (SPR 2016), 2016. URL https://hal.archives-ouvertes.fr/hal-01376998.

H. Hadsell, S. Chopra, and Y. LeCun. Dimensionality reduction by learning an invariant mapping. In 2006 IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR’06), volume 2, pages 1735–1742, 2006. doi: 10.1109/CVPR.2006.100.

A. Hatamizadeh, Y. Tang, V. Nath, D. Yang, A. Myronenko, B. Landman, H. R. Roth, and D. Xu. UNETR: Transformers for 3D medical image segmentation. In 2022 IEEE/CVF Winter Conference on Applications of Computer Vision (WACV), pages 1748–1758, 2022. doi: 10.1109/WACV51458.2022.000181.

X. He, C. Tan, Y. Qiao, V. Tan, D. Metaxas, and K. Li. Effective 3D humerus and scapula extraction using low-contrast and high-shape-variability MR data. In Medical Imaging 2019: Biomedical Applications in Lecture, Structural, and Functional Imaging – Volume 10953, pages 118–124. SPIE, 2019. doi: 10.1117/12.2513107.

A. Hirschmann, J. Cyriac, B. Stieljes, T. Kober, J. Richardi, and P. Omoumi. Artificial intelligence in musculoskeletal imaging: Review of current literature, challenges, and trends. Seminars in Musculoskeletal Radiology, 23(3):304–311, 2019. ISSN 1098-898X. doi: 10.1055/s-0039-1684024.

J. Hu, L. Shen, S. Albanie, G. Sun, and E. Wu. Squeeze-and-excitation networks. IEEE Transactions on Pattern Analysis and Machine Intelligence, 42(8):2011–2023, 2020. ISSN 1939-3539. doi: 10.1109/TPAMI.2019.2913372.

X. Hu, D. Zeng, X. Xu, and Y. Shi. Semi-supervised contrastive learning for label-efficient medical image segmentation. In M. de Bruijine, P. C. Cattin, S. Cotin, N. Padoy, S. Speidel, Y. Zheng, and C. Essert, editors, Medical Image Computing and Computer Assisted Intervention – MICCAI 2021, Lecture Notes in Computer Science, pages 239–249. Springer International Publishing, 2021b. ISBN 978-3-030-87193-2. doi: 10.1007/978-3-030-87193-2_23.
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O. Russakovsky, J. Deng, H. Su, J. Krause, S. Satheesh, S. Ma, Z. Huang, A. Karpathy, A. Khosla, M. Bernstein, A. C. Berg, and L. Fei-Fei. ImageNet large scale visual recognition challenge. *International Journal of Computer Vision*, 115(3):211–252, 2015. ISSN 1573-1405. doi: 10.1007/s11263-015-0816-y.

E. Schneider, A. Horváth, G. Rauter, A. Zam, M. Müller-Gerb, and P. C. Cattin. 3d segmentation networks for excessive numbers of classes: Distinct bone segmentation in upper bodies. In M. Liu, P. Yan, C. Lian, and X. Cao, editors, *Machine Learning in Medical Imaging*, Lecture Notes in Computer Science, pages 40–49. Springer International Publishing, 2020. ISBN 978-3-030-59861-7. doi: 10.1007/978-3-030-59861-7_5.

C. Shen, P. Wang, H. R. Roth, D. Yang, D. Xu, M. Oda, W. Wang, C.-S. Fuh, P.-T. Chen, K.-L. Liu, W.-C. Liao, and K. Mori. Multi-task federated learning for heterogeneous pancreas segmentation. In C. Oyarzun Laura, J. M. Cardoso, M. Rosen-Zvi, G. Kaisiss, M. G. Linguraru, R. Shekhar, S. Wescar, M. Erdt, K. Drechsler, Y. Chen, S. Albarqouni, S. Babak, B. Landman, N. Rieke, H. Roth, X. Li, D. Xu, M. Gabrani, E. Konukoglu, M. Guindy, D. Rueckert, A. Ziller, D. Usynin, and J. Passerat-Palmbach, editors, *Clinical Image-Based Procedures, Distributed and Collaborative Learning, Artificial Intelligence for Combating COVID-19 and Secure and Privacy-Preserving Machine Learning*, Lecture Notes in Computer Science, pages 101–110. Springer International Publishing, 2021. ISBN 978-3-030-90874-4. doi: 10.1007/978-3-030-90874-4_10.

L. Song, J. Lin, Z. J. Wang, and H. Wang. An end-to-end multi-task deep learning framework for skin lesion analysis. *IEEE Journal of Biomedical and Health Informatics*, 24(10):2912–2921, 2020. ISSN 2168-2208. doi: 10.1109/JBHI.2020.2973614.

C. Szegedy, V. Vanhoucke, S. Ioffe, J. Shlens, and Z. Wojna. Rethinking the inception architecture for computer vision. In 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), pages 2818–2826, 2016. doi: 10.1109/CVPR.2016.308.

M. Tan and Q. Le. EfficientNet: Rethinking model scaling for convolutional neural networks. In *Proceedings of the 36th International Conference on Machine Learning*, pages 6105–6114. PMLR, 2019. URL: https://proceedings.mlr.press/v97/tan19a.html.

V. V. Valindria, N. Pawlowski, M. Rajchl, I. Lavdas, E. O. Aboagye, A. G. Rockall, D. Rueckert, and B. Glocker. Multi-modal learning from unpaired images: Application to multi-organ segmentation in CT and MRI. In *2018 IEEE Winter Conference on Applications of Computer Vision (WACV)*, pages 547–556, 2018. doi: 10.1109/WACV.2018.00066.

J. Wang, C. Lan, C. Liu, Y. Ouyang, T. Qin, W. Lu, Y. Chen, W. Zeng, and P. S. Yu. Generalizing to unseen domains: A survey on domain generalization. *Machine Learning in Medical Imaging*, Lecture Notes in Computer Science, pages 101–110. Springer International Publishing, 2021. ISBN 978-3-030-90874-4. doi: 10.1007/978-3-030-90874-4_10.

Q. Zhang, Y. N. Wu, and S.-C. Zhu. Interpretable convolutional neural networks definition. *arXiv:2103.02503 [cs]*, 2021.

Q. Zhang, Y. N. Wu, and S.-C. Zhu. Interpretable convolutional neural networks. In *CVF Conference on Computer Vision and Pattern Recognition*, pages 8827–8836, 2018. doi: 10.1109/CVPR.2018.00920.

K. Zhou, Z. Liu, Y. Qiao, T. Xiang, and C. C. Loy. Domain generalization in vision: A survey. *arXiv:2103.02503 [cs]*, 2021.

Z. Zhou, G. Zhao, R. Kijowski, and F. Liu. Deep convolutional neural network for segmentation of knee joint anatomy. *Magnetic Resonance in Medicine*, 80(6):2759–2770, 2018. ISSN 0740-3194. doi: 10.1002/mrm.27229.

Y. Zhu, Y. Tang, Y. Tang, D. C. Elton, S. Lee, P. J. Pickhardt, and R. M. Summers. Cross-domain medical image translation by shared latent gaussian mixture model. In A. L. Martel, P. Abolmaesumi, D. Stoyanov, D. Mateus, M. A. Zuluaga, S. K. Zhou, D. Racoeceanu, and L. Joskowicz, editors, *Medical Image Computing and Computer Assisted Intervention – MICCAI 2020*, Lecture Notes in Computer Science, pages 379–389. Springer International Publishing, 2020. ISBN 978-3-030-59713-9. doi: 10.1007/978-3-030-59713-9_37.

Supplementary Materials

Metrics definition

Let $GT$ and $P$ be the ground truth and predicted 3D segmentation masks and let $S_{GT}$ and $S_P$ be the surface voxels of the corresponding sets. The metrics were defined as follows:

\[
\text{DICE} = \frac{2|GT \cdot P|}{|GT| + |P|} \tag{S1}
\]

\[
\text{Sensitivity} = \frac{|GT \cdot P|}{|GT|} \tag{S2}
\]

\[
\text{Specificity} = \frac{|GT \cdot \bar{P}|}{|\bar{GT}|} \tag{S3}
\]

\[
\text{MSSD} = \max(h(S_{GT}, S_P), h(S_P, S_{GT})) \tag{S4}
\]

with $h(S, S') = \min_{s \in S, s' \in S'} \|s - s'\|_2$

\[
\text{ASSD} = \frac{1}{|S_{GT}| + |S_P|} \left( \sum_{s \in S_{GT}} d(s, S_P) + \sum_{s \in S_P} d(s, S_{GT}) \right) \tag{S5}
\]

with $d(s, S') = \min_{s' \in S'} \|s - s'\|_2$

\[
\text{RAVD} = \frac{|GT| - |P|}{|GT|} \tag{S6}
\]

Distance measures were transformed to millimeters using voxel size information extracted from DICOM metadata.