Predicting pain duration or pain intensity from patellofemoral pain maps using deep learning models

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Abstract

Introduction: *Patellofemoral pain (PFP) syndrome is a musculoskeletal condition that presents as pain behind or around the patella without known structural changes [1]. Partial correlations between perceived size of PFP from pain maps and pain duration along with pain intensity has been indicated in previous studies [2], however, morphology and location of PFP remains unexplored in terms of correlation. Based on the object detection capabilities of deep learning methods, they may be used to detect image-features related to morphology and location. The aim of this study was to determine the performance of deep learning models for predicting pain duration and pain intensity, based on morphology and location of perceived PFP from pain maps.*

Methods and materials: *PFP drawings were collected on a body-schema and encoded into three different pain map representations in respect of morphology of pain, a location of pain, and a combination of morphology and location. The distributions of pain duration and pain intensity were analysed and used for defining the classification intervals for pain duration, to which the intervals were 0-12 months and 36-300 months, and pain intensity, 0-4 and 8-10 on VAS. Estimation of generalization performance of the models was calculated during the testing.*

Results: *The results of the test showed a higher accuracy for pain intensity classification than pain duration classification using the combined-representation. Pain intensity had an accuracy of 86.67%, and pain duration had an accuracy of 55.56%. However, the morphology-representation resulted in the highest predictive value classifying according to pain duration. The models using the location-representation had the lowest classification performance according to both pain duration and pain intensity, compared to the two other representations.*

Discussion: *Despite pain intensity being defined as multidimensional and subjective, the performance accuracy was higher than pain duration. The results may indicate that a combination of the morphology and the location of the pain had a higher classification performance in relation to pain intensity. Currently, it is unclear if deep learning methods may be a suitable approach for classifying PFP syndrome to work as support in clinical settings, to which further optimization of the models is necessary. Improvements could be found when more pain maps become available to better reflect generalization patterns in PFP drawings.*

1. Introduction

Patellofemoral pain (PFP) syndrome is a painful musculoskeletal condition that is presented as pain behind or around the patella [3, 4]. PFP syndrome affects 6-7% of adolescents, of whom two-thirds are highly physically active [5]. Additionally, the prevalence is more than twice as high for females than males [5, 1]. PFP syndrome is typically present over a longer period of time where a high number of individuals experience a recurrent or chronic pain [6]. Chronic pain may be maintained by the phenomenon central sensitization, which may result in widespread pain over time. Ultimately, PFP syndrome may lead to osteoarthritis [1, 7].

PFP is often described as diffuse knee pain, that can be hard for individuals to explain and localize [6]. Despite that individuals feel pain in the knees, there is no underlying structural changes to be found such as significant chondral damage. There is no definitive clinical test to diagnose PFP syndrome and is thereby often diagnosed based on exclusion criteria [1], to which PFP syndrome is also described as an orthopaedic enigma, and is one of the most challeng-

ing pathologies to manage [8]. To assist diagnosis of PFP syndrome, pain maps may be used as a helpful tool for the individuals to communicate their pain by drawing the perceived pain areas on a body outline [9].
A study by Boudreau et al. [2] indicates, through the use of pain maps (n=35), that there is a correlation between the size of the pain areas (total number of pain pixels) and the pain duration as well as pain intensity for individuals with PFP duration longer than five years.[2] However, it is unknown whether pain duration has an influence on the morphology of the pain and location, as well as whether the morphology of pain and location have an influence on pain intensity. The relation between pain maps and pain duration or pain intensity may be complex because the perceived PFP is subjective, and considered as multifactorial [10]. Additionally, the study by Boudreau et al. [2] did not find a correlation between 35 pain maps and pain duration or pain intensity for individuals with a pain duration below five years. To investigate whether there are patterns to be found in pain maps according to pain duration or pain intensity, a deep learning method was used. This method has not previously been applied to this type of data.
The aim of this study was to explore how accurate a deep learning model could classify pain maps according to pain duration or pain intensity. It was assumed that the models classifying according to pain duration would have a higher predictive value than pain intensity, because of the subjectivity of pain, and its possibility of being multifactorial. The pain maps were encoded into multiple pain map representations to investigate the performance of the models using different representations. Representations reflecting the morphology of the pain and the location of the pain were created. It was assumed that a deep learning model would perform better with more features, thus a combined representation containing morphology and location of the pain was made. The representations are referred to as morphology- (MR), location- (LR), and combined-representation (CR).

2. Methods

This section presents the pain maps and preprocessing, to which the pain maps are encoded in three different representations. Furthermore, the architecture of the deep learning models are presented, followed by a description of how the models were trained and optimized. Finally, the linearity of the pain maps is tested to compare the performance of simple linear models to deep learning models.

2.1. Pain maps

Pain maps used in this study were collected from a Danish ACTNODE study, and from an on-going clinical trial (FOXH) which is conducted in collaboration with Danish and Australian universities. The pain maps were drawn by individuals with PFP syndrome through the use of an application, Navigate Pain, in a clinical setting.
Navigate Pain is a software application that is used to visualize the location, morphology, and spatial distribution of pain from individuals to healthcare personnel. The application permits individuals to draw their pain with different colors and line thickness onto a body outline, an example is shown in Fig. 1.

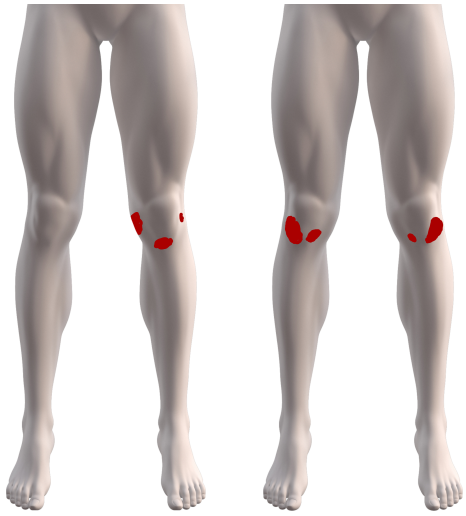

Fig. 1: *Pain maps from two individuals with uni- and bilateral PFP. The red markings indicate the area of pain perceived by the individuals.*

The number of pain maps associated with pain duration was 205, and 197 associated with pain intensity measured according to the Visual Analog Scale (VAS). In order to improve the performance of the deep learning models, gender was included as an additional input. This was chosen because females tend to report more intense and frequent pain than males [11].

2.2. Pre-processing of pain maps

The pain maps were processed in MatLab v. R2017b, where the images were resized, since they were collected with different resolutions (screen sizes) and cropped to only include the knees. To increase the amount of pain maps, a split body approach was chosen because deep learning models may benefit while using a larger dataset. Using the split body approach, the knees in the pain maps were separated into a single knee pain image. The left knee was then mirrored to resemble the right knee to minimize the variance in the images. The final pain maps had resolutions of 252×118 pixels. By using split body approach it was assumed that the pain duration and pain intensity were identical for both knees if PFP was bilateral. This resulted in an increased total number of pain maps with gender and pain duration to 333, and pain maps with gender and pain intensity to 319.
The models were designed to classify pain maps according to pain duration or pain intensity divided into two classes with intervals based on the extremes. The classification intervals were 0 to 12 months and 36 to 300 months for pain duration, and 0 to 4 and 8 to 10 for pain intensity measured on VAS. The reason for choosing extreme intervals, was to separate closely related patterns between the two classes, which resulted in the number of pain maps as shown in Table 1.

	Pain duration (months)		Pain intensity (VAS)	
	0-12	36-300	0-4	8-10
MR	114	122	72	124
LR	105	118	68	118
CR	113	121	71	123

Table 1: *The number of pain maps for MR, LR, and CR for both pain duration and pain intensity using the extremes.*

2.2.1 Morphology-representation (MR)

The original pain maps reflect the morphology of the pain, which refers to its shape and distribution. The original pain maps were converted into binary matrices, where the pain was indicated with "1" and no pain as "0". This representation did not require further processing than converting the pain maps to a matrix including gender and the output, pain duration or pain intensity.

2.2.2 Location-representation (LR)

A simplified representation of the pain maps was created to investigate whether the location has patterns related to the pain duration or pain intensity. The location of the pain was reflected by the use of knee regions shown in Fig. 2, where the regions are based on the underlying anatomical structures. The location were divided into ten regions, which were inspired by Photographic Knee Pain Map (PKPM). The divisions were designed to categorize location of knee pain for diagnostic and research purposes.[12]

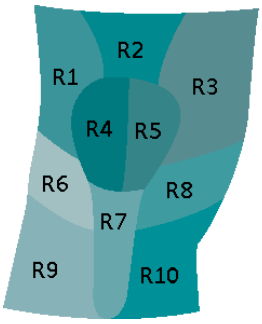

Fig. 2: *The regions of the right knee (R1-R10).*

There are ten regions, where regions 1 and 3 represent the superior lateral and superior medial areas for patella. Region 2 refers to quadriceps tendon. The patella is divided into lateral and medial regions, which are regions 4 and 5. Regions 6 and 8 are lateral and medial joint line areas. Patella's tendon is region 7 and the two last regions, 9 and 10, are tibia lateral and medial.[12]
A vector consisting of ten elements was created, where each value represented either an active region (1) or a not active region (0). The values were defined by using a threshold to determine whether a region was considered active in relation to the amount of pain pixels in the specific region. The threshold was used to accommodate for the diffuse pain and the difficulty in localizing PFP. The threshold increased the confidence of an active pain region by avoiding minimal contributions. Simultaneously, the threshold should not be too high so too many or big areas were excluded. The threshold indicated which minimal percentage of pain pixels, that should be present in a specific region before it was considered as active. The threshold was decided based on an analysis of five random pain maps, where threshold values of 0, 5, 10 and 15% were

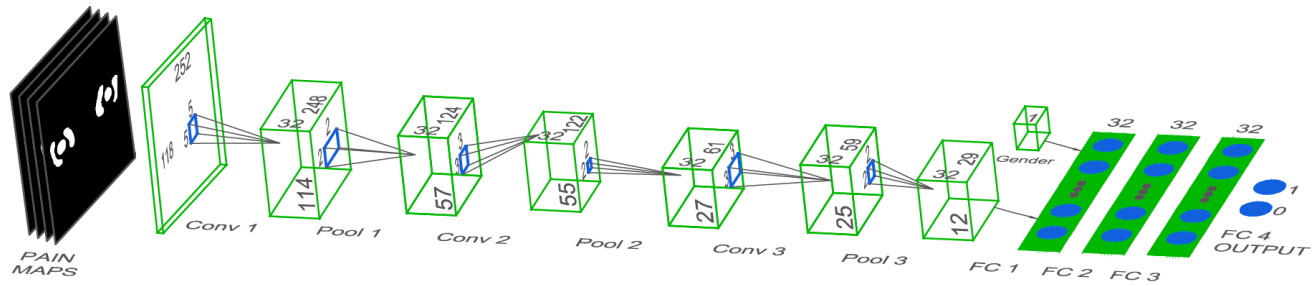

Fig. 3: *The architecture of the deep learning models including the MR before optimization. The models consisted of three convolutional, three max pooling, and four fully connected layers. The gender was included in the first fully connected layer. The boxes represent the output after each layer.*

compared. Based on the analysis, a 5% threshold was chosen.

2.2.3 Combined-representation (CR)

A combination of morphology and location of the pain was created based on components from MR and LR. The original pain maps were superimposed on the knee regions, which resulted in pain pixels reflecting the location with a number from one to ten. Before using the representation as input in the deep learning models, a one-hot encoding approach was used, which made it possible to separate categorical data into binary data [13]. As a result, the ten values did not have a relation to each other when analysed in the deep learning models.

2.3. Architecture of the deep learning models

Deep learning models were developed on a computer with 4x "Intel® Core^{TM} i7" CPUs and one single GPU of type "Geforce GTX 970M", using the programming language Python v3.6.3. Libraries used was Keras v2.0.8 with a TensorFlow v1.3.0 backend.
Six deep learning models for the three pain map representations and pain duration or pain intensity were created. The models used supervised learning, which is defined as a network learning to classify a given input corresponding to a specific output [14]. The models were designed differently according to each pain map representation and type of classification. The architecture of the models, before optimization, including the MR is illustrated in Fig. 3. The models classified MR and CR consisted of three convolutional layers, to which a max pooling layer was added after each convolutional layer, and followed by four fully connected layers, where gender was inserted as a secondary input for the models. The only difference in the models using the CR was the input image, which was represented as a matrix with ten layers. The models including LR consisted of only four fully connected layers of the architecture shown in Fig. 3.

2.3.1 The convolutional layers

Convolutional Neural Networks (CNNs) is a type of neural network for processing data with a grid-like topology [14]. CNNs were used to classify MR and CR because of its capability to perform highly according to image classification. The purpose of the convolutional layers was to recognize features in the pain maps by taking the image and scan it, and then split it up into feature maps.[14, 15] The first convolutional layer consisted of a kernel size of 5×5 and 32 filters. The two following convolutional layers consisted of kernel sizes on 3×3 and 32 filters.

2.3.2 Max pooling layers

For the models containing convolutional layers, each convolution layer was followed by a max pooling layer, which is a typical structure of a convolutional network [14, 16]. Max pooling layers are used to reduce the size of the dataset, while maintaining features from the feature maps. Given a reduction in the data, the computation speed may increase.[14, 15] Max pooling layers were defined after each convolutional layer, to which all have a kernel size of 2×2 with a stride of 2. From the kernel window, the highest of the 4 values was extracted to next layer and used further through the network.

2.3.3 Fully connected layer and output layer

All the models consisted of four fully connected layers, where the first layer received a flattened version of the input. The notation for gender was included in the end of the array, which was used as input in the first fully connected layer with 32 nodes. Additionally, the second and third layers consisted of 32 nodes. The fourth fully connected layer, which also was the output layer, included a sigmoid activation function. This function operates with a single output, that saturates when its input is either extremely negative or extremely positive [14]. The single output refers to the number of classification intervals, pain duration 0-12 month, and 36-300 months, or pain intensity 0-4, and 8-10 on VAS.

2.3.4 Rectified Linear Unit activation function

The activation function, chosen for all hidden layers in the models, was Rectified Linear Unit (ReLU), which transforms the linear output to a nonlinear function by making all negative values to zero. The ReLU function still remains nearly linear, which means it can easily be optimized with gradient descent based methods. In modern neural networks, ReLU is recommended to use as a default activation function and could be defined as $g(x) = max\{0, x\}$.[14]

2.3.5 Dropout algorithm

A dropout algorithm was implemented for the models in the first two hidden fully connected layers to reduce overfitting while training. The algorithm works by randomly dropping a specified fraction of the nodes in the given layer, to which the nodes that drop, and changes between different nodes during the training [17]. Dropout reduces the nodes' ability for co-adaptation, where multiple nodes compute the same features. For the models, the dropout fraction was set to 0.5 (50%) based on a previous study by Srivastava et al. [17], which found 0.5 as optimal for multiple ranges of networks.

2.3.6 Back-propagation algorithm

Back-propagation was used for the learning process where the weights of the models were adjusted in order to reduce the error calculated between the predicted output, and the correct output [18]. Back-propagation is based on gradient descents, which computes gradients from the output to the input, in order to minimize the overall output error as much as possible during the learning stage. After each pass of a minibatch, the inputs and weights were multiplied for each node summed with additional coefficient bias.[15, 19] Afterwards, a loss was calculated based on a loss function for every input that passed through the network to make the adjustments on the parameters to reduce the loss. As training progressed, the loss should decrease as a result of the parameter updates, and improve the performance of the neural network.[14, 16, 18] This learning process continued until optimal parameters with minimum error were reached.[19]

2.4. Training of the models

The models were trained and optimized with a structured grid search of hyperparameters to help set the initial parameters for the models. These hyperparameters refer to learning rate, number of filters and nodes, and number of epochs with different batch sizes. Accuracy was used to determine the improvement of performance when testing the multiple parameters. Further, the pain maps were divided into three subsets, a training set consisting of 75%, a validation set consisting of 10%, and a test set of the remaining 15%. A manual optimization was performed, using the validation set, by evaluating the development in loss, accuracy during training, and the general performance estimated from accuracy. After optimization, the models were tested with the test set, using the hyperparameters from the optimization.

2.5. Nonlinearity in pain maps

Additionally, linear regressions were made to validate whether the deep learning models used more than the simple features to predict either pain duration or pain intensity. Given that PFP is subjective and multifactorial it is unlikely that the pain maps and pain intensity are linearly correlated. In order to determine if there was indeed a linear relationship, linear regressions were done on simple features reflecting the size of the pain and number of active pain regions. Linear regressions were made in MatLab, and composed correlations between; number of pain pixels and pain duration, number of pain pixels and pain intensity, number of active pain regions and pain duration, and number of active pain regions and pain intensity.

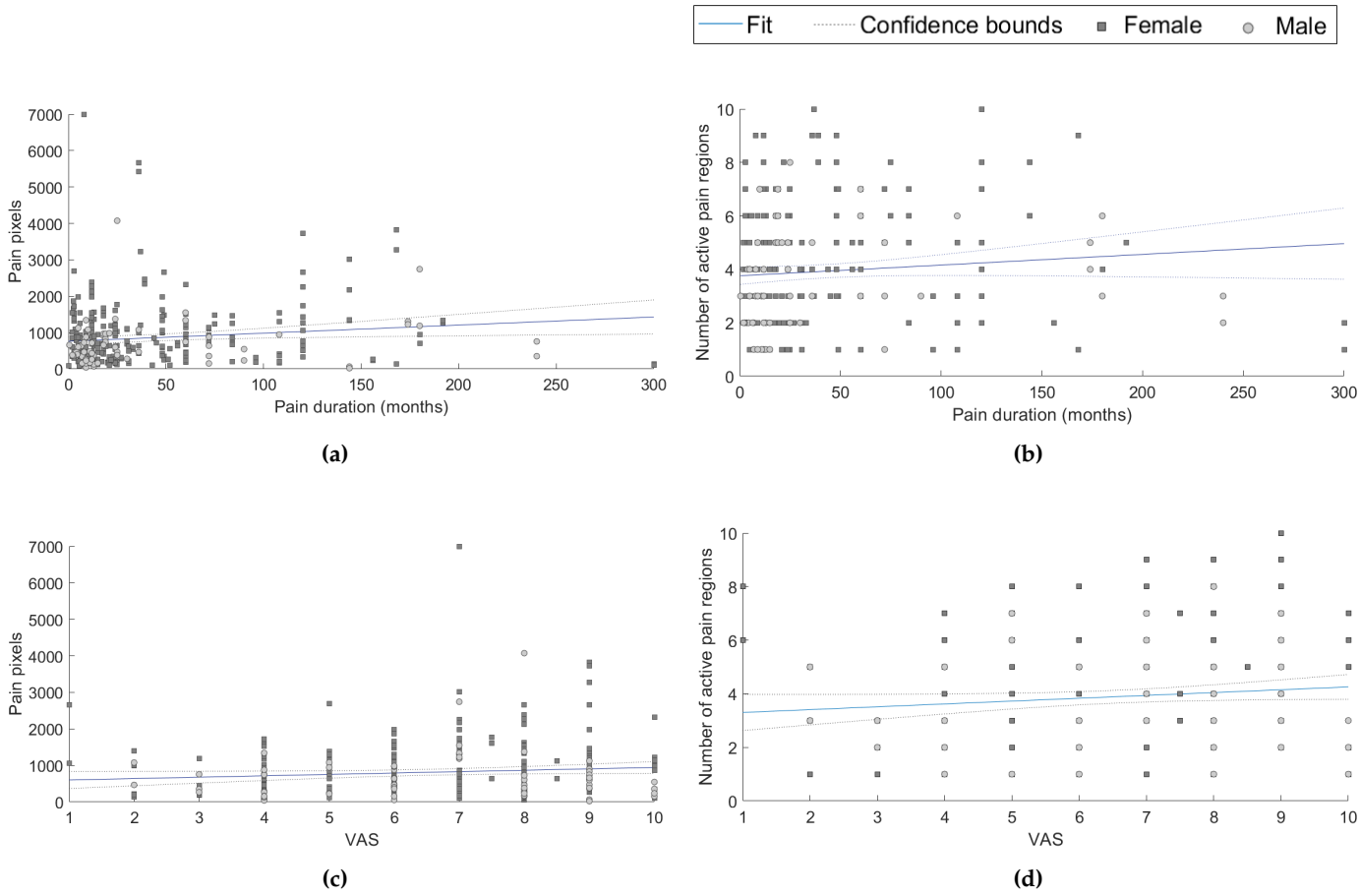

Fig. 4: *Linear correlations of pain pixels and pain duration (a), active pain regions and pain duration (b), pain pixels and pain intensity indicated in VAS (c), and active pain regions and pain intensity indicated in VAS (d).*

3. Results

The linear regressions between simple features, number of pain pixels or active pain regions, and pain duration or pain intensity, resulted in the plots shown in Fig. 4. The R^2-values indicated a poor fit according to the linear regression lines. The regression for the correlation in Fig. 4a resulted in $R^2 = 0.018$, Fig. 4b $R^2 = 0.008$, Fig. 4c $R^2 = 0.011$ and Fig. 4d $R^2 = 0.011$.

3.1. Optimization of the models

During the optimization, a structured grid search resulted in different hyperparameters according to each model, which is shown in Table 3.

	Learning rate	Nodes	Epochs/ Batch size
MR: Pain duration	0.01	64	120/20
MR: Pain intensity	0.1	16	140/10
LR: Pain duration	0.01	16	120/20
LR: Pain intensity	0.01	16	120/20
CR: Pain duration	0.1	16	120/30
CR: Pain intensity	0.001	16	120/30

Table 3: *Hyperparameters for each model after initial grid search.*

For the deep learning models including MR different hyperparameters were used to obtain the highest performance. The models including LR had similar results from the optimization. Furthermore, the model including CR had almost identical hyperparameters except for the learning rate.

3.2. Performance of the models

The accuracy, sensitivity, and specificity of the models during test according to the representations are shown in Table 2. Furthermore, confusion matrices were created according to the pain duration as shown in Fig. 5, and confusion matrices according to pain intensity as shown in Fig. 6. The models that used MR resulted in a higher predictive value for pain duration and pain intensity in the higher extremes (36-300 months and 8-10 VAS), compared to the lower extremes (0-12 months and 0-4 VAS). By comparing the sensitivity and specificity of the model using MR to predict pain duration or pain intensity, the pain duration had a higher predictive value according to the true low pain duration, and true high pain duration. Overall, the models using LR, could not predict according to the lower extremes but classified only according to the higher extremes. The model using CR to predict pain intensity, resulted in the best performance, based on the accuracy, sensitivity, and specificity, thus the model predicted better to the higher extremes. The model with the highest accuracy of 86.67% was the model using CR to predict pain intensity, whereas the lowest accuracy of 35.29% was the model using LR predicting according to pain duration.

4. Discussion

This section discusses the split body approach, the models' performance according to the multiple pain map representations, and limitation of using threshold to create LR. Finally, a possible optimization of the deep learning models is discussed.

	Accuracy (%)	Sensitivity (%)	Specificity (%)
Morphology-representation (MR)			
Pain duration	69.44%	56.25%	80.00%
Pain intensity	60.00%	40.00%	75.00%
Location-representation (LR)			
Pain duration	35.29%	0.00%	100%
Pain intensity	60.71%	0.00%	100%
Combined-representation (CR)			
Pain duration	55.56%	55.00%	43.75%
Pain intensity	86.67%	75.00%	90.91%

Table 2: *Generalization performance of the models, which used the MR, LR, and CR test subset when classifying according to pain duration or pain intensity.*

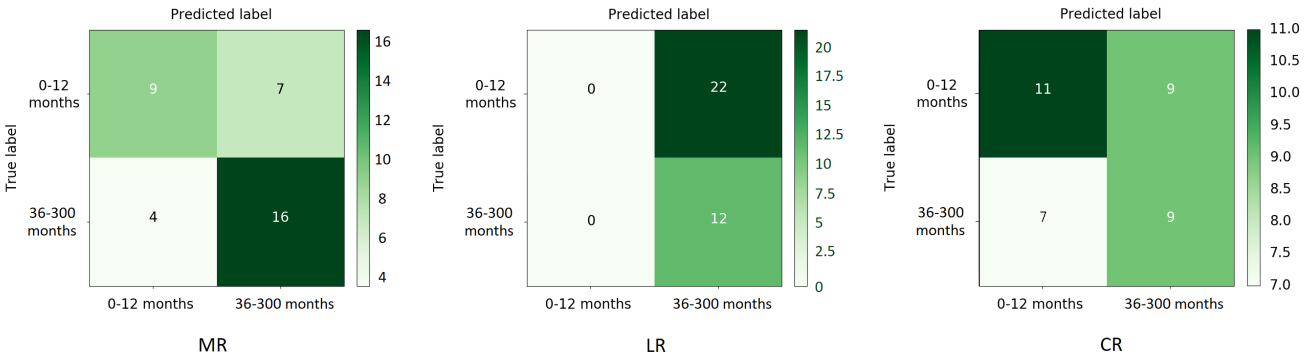

Fig. 5: *Confusion matrices of MR classified according to pain duration, LR classified according to pain duration, and CR classified according to pain duration.*

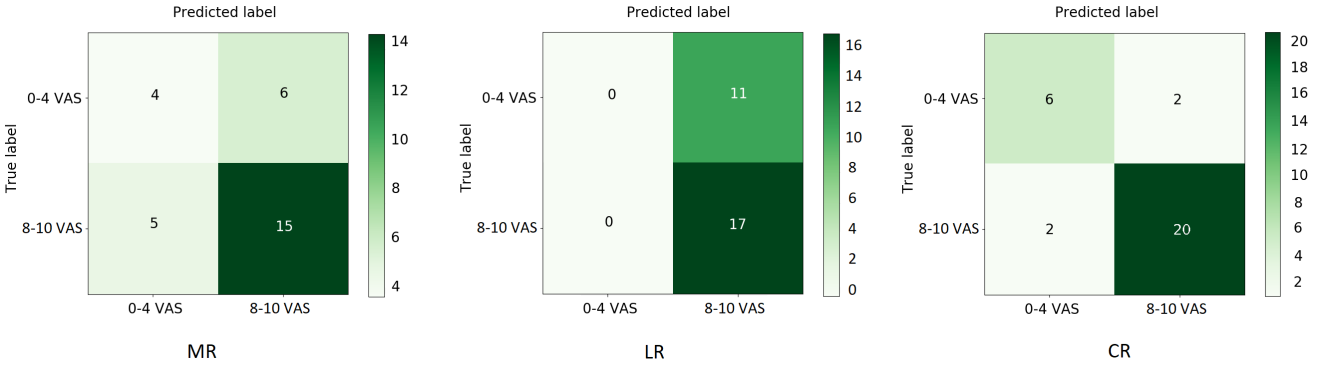

Fig. 6: *Confusion matrices of MR classified according to pain intensity, LR classified according to pain intensity, and CR classified according to pain intensity.*

4.1. Consequences of using split body

In this study, the total number of pain maps was 217 from the individuals with uni- and bilateral PFP. Comparing to the literature, a supervised deep learning model should use five thousand labeled data per category to obtain an acceptable performance [14]. The number of pain maps was not optimal, to which a split body approach was used to increase the size of the dataset. However, this approach combined with the mirroring of pain, may have resulted in pain maps being incorrectly labeled. This could be the case for the pain map shown in Fig. 7(a), where there is a clear difference in size of pain areas, morphology, and location of the pain between the two knees.

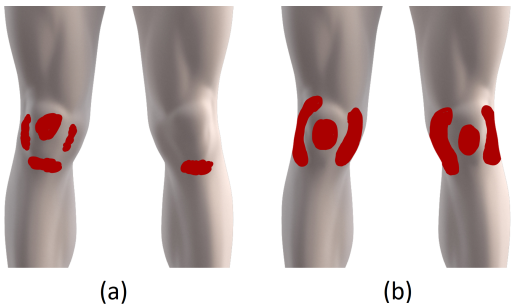

Fig. 7: *Pain maps for (a) asymmetric PFP, and (b) symmetric PFP.*

Theoretically, the PFP may have occurred on one leg first, and afterwards have spread to the other knee, which could affect the pain duration. Furthermore, the individual may feel more pain in one of the knees, which could affect the pain intensity value. Moreover, several pain maps had nearly symmetrical pain drawn on both knees, as shown in Fig. 7(b), which could result in the models using nearly identical pain maps for training as well as testing.
The consequences of using this approach may have resulted in multiple incorrect labeled pain maps, which may be reflected in the pain map representations. Furthermore, this may have influenced the training of the models, and therefore the performance results, which may be misleading according to the original pain maps. Ideally, a split body approach should not be used if a larger amount of pain maps become available.

4.2. Classification of pain maps

The linear correlations showed a poor fit according to the regression lines. When comparing the linear regressions to the deep learning models, it is assumed that the models utilizes more than just the simple feature (pain pixels or active pain regions) of the pain maps. The results from testing the models, showed that the model classifying CR according to pain intensity had the highest accuracy, whereas the model classifying LR according to pain duration scored the lowest accuracy. Additionally, the sensitivity and specificity needs to be considered, given that if either sensitivity or specificity is zero-valued, the accuracy only reflects the total number of pain maps in one given class.
The models including MR were able to predict according to both lower and higher extremes, which may indicate that there is a pattern to be found in this representation. Additionally, there is an indication of more patterns to be found in the higher extremes. This may support the finding in the study by Boudreau et al. [2], showing a partial correlation between pain maps and

pain duration or pain intensity for individuals with PFP longer than five years. The results of the models using LR could not distinguish between the pain maps according to the extremes for both pain duration and pain intensity. The models simply classified all pain maps as being in the higher classes, indicating that no patterns were learned for the lower extreme classifications, for both pain duration and pain intensity. It can be as a result of the simplified representation of the location, which did not present the size of the pain, only the active region. The models using CR resulted in the highest performance when predicting pain intensity, according to the accuracy, sensitivity, and specificity. This may be a result of more patterns to be found in the CR because it includes features from both morphology and location of the pain. Overall, the models performed better when classifying higher intervals, which might be a result of the imbalance of the pain maps with lower and higher pain durations and pain intensities. This imbalance can be seen in Table 1, where the higher classes contain more pain maps. The models predicting pain duration from MR had the highest accuracy, suggesting that the MR may contain more beneficial features for predicting according to pain duration than pain intensity. However, pain intensity had a higher predictive value in relation to CR, than pain duration, which may be a result of CR having more beneficial features to predict pain intensity. The performance accuracy, when using LR, shows that it had the lowest performance, since it only could predict according to the higher extremes, which makes it the least recommended representation of pain maps for predicting either pain duration or pain intensity.

4.3. Limitation of threshold

The LR had a 5% threshold that defined when a pain region was considered active according to the amount of pain. It can be discussed whether this threshold was suitable, since adding the threshold resulted in loss of pain maps that had a very small amount of pain. However, a smaller threshold or no threshold would give active pain regions that might only contain very few pain pixels. Since PFP is described as hard to localize, it is unknown how precise the individuals have drawn their pain, thus every pixels should maybe not be taken into account. The CR did not have a threshold for defining active pain regions, because the morphology of the pain would be affected when discarding small pain areas. This representation is thereby not a complete combination of the MR and LR. A threshold could be applied for CR as well, to which additional threshold values to preserve the morphology of pain should be explored.

4.4. Optimization of deep learning models

Optimization of the deep learning models is often a time-consuming process based on the picks of the multiple hyperparameters and different algorithms which could be implemented during the development of the models. Activation functions were chosen based on the literature, where ReLU should be used for convolutional and fully connected layers in neural network models, and sigmoid should be picked for binary output layer. However, additional testing could be made by using softmax or linear activation function to increase the generalization performance of the models. The dropout algorithm was set to the default 0.5 and used in all models in the fully connected layers to turn off the amount of nodes and prevent the models from overfitting. Additional values could have been tested in order to find the most optimal values for every model. Unfortunately, the lack of time and time-consuming reruns during every optimization cycle, lead to use the common hyperparameters as there were many others which were tested with grid search 10-fold cross-validation. Additional limitation of this study was the lack of computational power which lead to a more simple architecture of the models, containing fewer layers and a lower range of hyperparameters. Thus, an improvement in performance may be found through more powerful systems or services.
A further optimization of the models may be found according to the input parameters, to which more physiological, physical and psychological features may increase the performance accuracy. Physiological and physical features, such as age, height, weight, physical activity level, and sports activity, may influence pain duration or pain intensity. Age could be a relevant feature since the perceived pain is dependent on the individual's personality and character. Younger individuals may feel more pain because of a new pain, than older individuals which have had PFP for a longer period of time. In addition, older individuals may feel more pain because of the phenomenon central sensitization, which in some cases may facilitate widespread pain. The physical activity level and sport may in-

crease the pain intensity for some individuals because of the patellofemoral loaded activity. The psychological factor is an important feature to consider, because of its influence on pain intensity. Pain is multifactorial and can be influenced by psychosocial factors [20]. Furthermore, other pain areas, such as hip pain, may influence the pain intensity of PFP.

5. Conclusion

This study predicted pain maps according to the pain duration or pain intensity. The model using the pain map representation reflecting both morphology and location of pain resulted in the highest accuracy according to pain intensity, despite the subjectivity of pain and the influence of multidimensional factors. The representation only including the location could not find patterns in the pain maps, to which this representation is not recommended. There may be an indication of patterns to be found between pain maps and pain duration or pain intensity, however further optimization, more pain maps or additional studies are needed to support whether location and morphology contain positive predictive value in terms of predicting pain duration or pain intensity.

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