Article

Determination of the cervical vertebra maturation degree from lateral radiography

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Abstract: Many environmental and genetic conditions may modify jaws growth. In orthodontics, the right treatment timing is crucial. This timing is a function of the Cervical Vertebra Maturation (CVM) degree. Thus, determining the CVM is important. In orthodontics, the lateral X-ray radiography is used to determine it. Many classical methods need knowledge and time to look and identify some features to do it. Nowadays, Machine Learning (ML) and Artificial Intelligent (AI) tools are used for many medical and biological image processing, clustering and classification. This paper reports on the development of a Deep Learning (DL) method to determine directly from the images the degree of maturation of CVM classified in six degrees. Using 300 such images for training and 200 for evaluating and 100 for testing, we could obtain a 90% accuracy. The proposed model and method are validated by cross validation. The implemented software is ready for use by orthodontists.

Keywords: Classification, orthodontics, Cervical Vertebra Maturation, Machin Learning, Artificial Intelligence, Deep Learning

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1. Introduction

1.1. Importance of the work and its interest for orthodontics community

Specialists in orthodontics are responsible for the treatment of dentofacial dysmorphisms, from different functional, genetical and morphological aetiologias. As a child or teenager is still growing, orthodontic treatment consists in a combination of orthodontics (about tooth position) and dentofacial orthopedics (about the guidance and stimulation of facial, maxilla and mandible growth in the three dimensions).

Many environmental and genetic conditions may induce upper or lower jaws lacks of growth. Classically, to handle a treatment properly, every etiological condition that can be modified or corrected, must be identified (diagnosis), normalized (treatment), and stabilized (retention). Specialists have to carefully examine and precisely analyze, all the medical, functional, clinical and radiographic data, in order to identify normal versus pathological conditions about tooth position, form or size, about lip, chin, cheeks, tongue and breathing functions, and about facial and jaws position and growing patterns. Adolescent orthodontic treatment also depends on proper management of jaws and facial growth, to allow a balanced jaws position, maximize the airway and improve the facial appearance. [1] Treatment planning in orthodontics depends on a systematic diagnosis and prognosis

Contemporary theories about craniofacial growth admit that the phenotype of the craniofacial complex is a result of a combination of genetic, epigenetic and environmental factors. The skeletal tissue of maxillomandibular complex is growing due to sutures and osteogenic cartilages proliferation depending on genetic, intrinsic and extrinsic environment. So facial growth can also be modified in amount and direction by extrinsic factors, including orthopedic and functional treatment. Thus, quantify facial and, in particular, mandibular growth remaining, influences diagnosis, prognosis, treatment goals and planning. Indeed, apart choosing the good appliance needed to change the rate and direction of jaw growth, the right treatment timing is crucial. If high growth rate is about to occur, orthopedic treatment may permit to correct jaws unbalanced, otherwise surgical correction of the jaws shift will be considered. The success of a dentofacial orthopedic treatment is linked to the determination of the best interventional frame (periods of accelerated or intense growth) to maximize the chances to reach skeletal goals, with adapted methods and devices, in an optimized duration.

The most common dentofacial dysmorphism, is the skeletal class II, corresponding to a short mandible. Study of normal mandibular growth and remodeling, has shown different ways of bone formation, that can be stimulated by functional and orthopedics treatments, in particular condylar growth responsible of 80% of the mandible growth. Numerous radiographic investigations have established that condylar/mandibular growth follows similar growth curve than statural growth.[2] This growth pattern is characterized by variations of growth rate in 4 stages: first a decrease of growth velocity from birth to 6 years old, then minor midgrowth spurt around 6 to 8 years, followed by a prepubertal plateau with decelerated growth rate, and finally the facial growth curve describe a peak of growth velocity corresponding at the pubertal growth spurt, which coincides, precedes or follows from 6 to 12 months the statural growth peak (controversial).[3] This spurt occurs approximately two years earlier in girls than in boys.[4]

To estimate mandibular growth potential left, the patient must be localized on is growth curve, and many biologic indicators have been proposed: increase in body height, menarche, breast and voice changes, dental development and eruption, middle phalanx maturation of the third finger, maturation of the hand and wrist, and cervical vertebral maturation. [3,7,8]

1.2. The classical radiographic manual methods

1.2.1. Hand-wrist radiograph method HWM:

The comparison method describes in the Atlas of Greulich et Pyle in 1959 or the Fishman's method in 1982, permit to identify specific ossification stages occurring before, during, or after mandibular growth peak, on left hand and wrist radiographs.[9,10] The hand wrist radiographs have been used as a gold standard in the assessment of skeletal maturation for many decades, but presented several issues as: the additional x-ray exposure, the time spending and experience required (even if a digital software is now available [11]), and a sexual dimorphism and ethnic polymorphism in morphological modifications.[12,13]

1.2.2. Vertebrae maturation CVM:

First who proposed to predict skeletal age and growth potential by cervical vertebrae maturation (CVM) method is LAMPARSKI in 1972. Cervical vertebrae are available on the lateral cephalometric radiographs, prescribed routinely by orthodontists for each patient diagnosis and treatment planning.[14] He has used measurements of mandibular length on several annual lateral cephalograms to describe individual mandibular growth curve, and correlated it with morphological description of vertebrae morphology at each stage. This method were modified several times first by Hassel and Farman (1995)[15], then twice by Baccetti et al. (2002 and 2005) for a more accurate assessment of cervical maturation, by 6 stages identified by morphological changes in the C2,C3,C4 vertebral bodies on a single lateral cephalogram, independently of patient gender. [16]

This last version is the most used nowadays to detect the mandibular growth spurt, as it shows the best results in clinical applicability.[17]

As every single bones of the human body, vertebrae growth and present maturational changes from birth to full maturity. Cervical vertebrae are the first seven pieces of the spinal column. Vertebral growth in the cartilaginous layer of the superior and inferior surfaces of each vertebrae, involves changes in size of vertebral bodies and shape of upper and lower borders of C2,C3,C4 vertebrae.

These changes have been described into 6 stages, correlating with morphological modifications of the vertebral shapes and estimated time lapse from the mandibular growth peak. Both visual and cephalometric appraisals of morphological changes have been proposed.

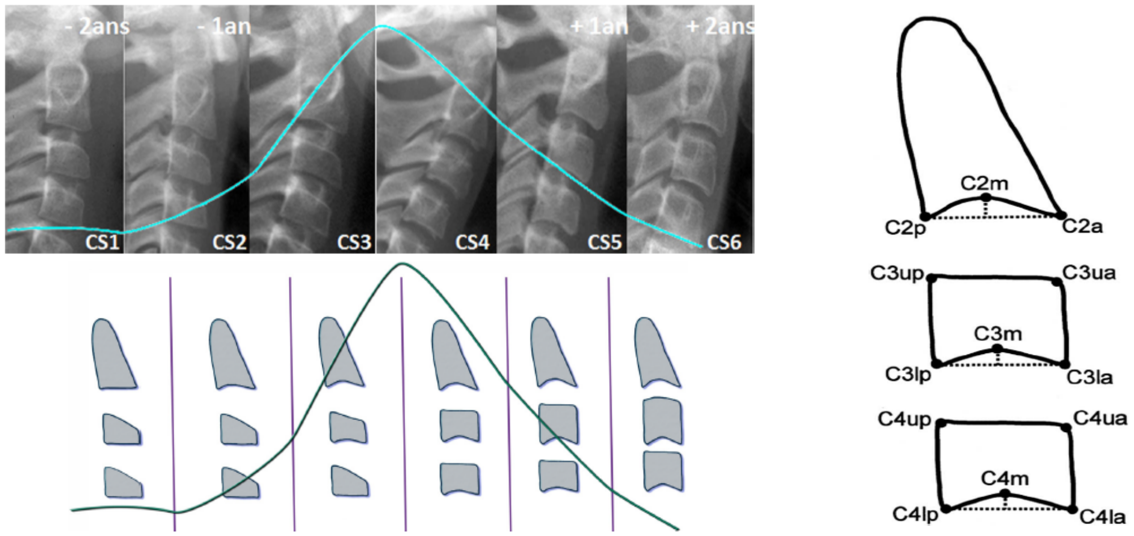

Figure 1. Left) CVM radiological and morphological stages superposed with Björk growth curve.[16], Right) Cephalometric landmarks for CVM stages determination.[1]

Visual analysis [1]:

- Cervical stage 1 (CS1) = 2 years before mandibular growth peak:
  Lower borders of C2 to C4 vertebrae are flat. C3 and C4 superior borders are tapered from posterior to anterior.
- Cervical stage 2 (CS2) = 1 year before mandibular growth peak:
  Lower border of C2 presents a concavity. Bodies of C3 and C4 are the same.
- Cervical stage 3 (CS3) = during the year of the mandibular growth peak:
  Lower borders of C2 and C3 present concavities. Vertebrae are growing so C3 and C4 may be either trapezoid or rectangular shape, as superior borders are less and less tapered.
- Cervical stage 4 (CS4) = 1 or 2 years after mandibular growth peak:
  Lower borders of C2, C3 and C4 present concavities. Both C3 and C4 bodies are rectangular with horizontal superior borders longer than higher.
- Cervical stage 5 (CS5) = 1 year after the end of mandibular growth peak:
  Still concavities of lower borders of C2, C3 and C4. At least one of C3 or C4 bodies are squared and spaces between bodies are reduced.
- Cervical stage 6 (CS6) = 2 years after the end of mandibular growth peak:
  The concavities of lower borders of C2 to C4 have deepened. C3 and C4 bodies are both square or rectangular vertical in shape (bodies higher than wide)

1.2.3. Cephalometric appraisals:

Using the landmarks illustrated on Figure 1(right), cephalometric analysis consists in the measurement of:

- The concavity depth of the lower vertebral border (estimated by the distance of the middle point (Cm) from the line connecting posterior to anterior points (Clp-Cla))
- The tapering of upper border of vertebral C3 and C4 bodies (estimated by the ratio between posterior and anterior bodies heights (Cup-Clp)/(Cua-Cla))
- The lengthening of vertebral bodies (estimated by the ratio between the bases length and anterior bodies borders height (Clp-Cla)/Cua-Cla)

Many researchers found this method as valid and reliable as hand and wrist Xray.[14] The cervical vertebrae maturation stages have been demonstrated as a clinically useful maturation indicators for evaluation of pubertal growth height and mandibular velocities [18,19,20], by correlation between chronological age and cervical vertebrae maturation, between hand-wrist and cervical-vertebrae maturation.[16,21,22,23]

Some studies underlined the need for association with other clinical assessments [24] in clinical practice, and a good reliability in differentiating pre and post mandibular growth spurt periods.[25]

1.3. The difficulties of the labeling task

Specific training is provided to assess CVM stages reliably, and repeatably at a satisfactory level.[26,27] Gabriel et al. minimized the risk of bias (radiographs without tracings, standardized training to private practice orthodontists...) and observed a moderate intra and inter-observer agreement (30 to 62% of cases). These results confirm the expertise required to proper determination of CVM stage, and may be explained by the use of a qualitative method of assessment, and the lack in detecting exceptional cases (individual variations in size and morphology, outside the norms defined by the method). Moreover, for orthodontists, the cervical vertebrae area on the lateral cephalograms is outside their expertise "visual field". They have poor general knowledge and experience about vertebrae observation, as they focus on maxillomandibular bones and teeth at first glance. This would have been a difficulty in the labeling task of our radiographs. All lateral radiographs have been labeled by a radiologic technician, specialized in cephalometric tracing and over trained in CVM stages agreement (3 years full time), using a standardized morphologic and cephalometric protocol. Intra observer reproducibility must be estimated in further study.

1.4. The need for automatization and the help which it brings

Estimation of CVM stage represents only one single element influencing the patient orthodontic treatment. The practitioner must master the entire clinical, functional, biomechanical and cephalometric data analysis in order to define proper diagnosis and treatment goals and planning. Even in being specialists, orthodontists require a very broad range of skills and a great deal of time for each patient complete diagnosis. Considering that reproducibility of classifying CVM stages is superior at 98% by trained examiners[1], automatization by expert eyes will provide time saving, efficiency, accuracy, repeatability in treatment planning and patient care.

Few studies have presented software programs for cephalometric determination of C2,C3 and C4 vertebrae proportions according reference points marked manually on the image, and automatically calculates the skeletal maturation stage. This computer-assisted analysis still depends on operator experience.[28]. Padalino et al run a study comparing manual analysis of CVM stages and the analysis performed by a dedicated software. It has shown a concordance of 94% between the two methods but hand-tracing analysis was quicker of 28 seconds on average.[29]

Deep learning conventional neural networks have already been used to diagnose metabolic disorders in pediatric endocrinology, in order to assess skeletal bone age on left hand-wrist radiographs. Deep learning approach proposes better accuracy than conventional methods in processing the image in less than 1 second. Our study aims to develop a fully automated deep learning assessment of CVM stages on lateral cephalograms in orthodontics.

2. Preprocessing of the data

For this classification task, we had an image data base of 2000 X ray radiographic images. Each image has a size of 2012x2012. These images are extracted from the patients files and are anonymized.

A selection of 600 images are studied and labelized by the experts in six classes (CVS1,...,CVS6). These labelized data are divided in three sets of Training, Validation and Testing. We did different division of the data: First, we had started by 300, 200 and 100, respectively for Training, Validation and

Testing. Then, we decided to divide them to 200, 200 and 200 and used Cross Validation technique by permutation of these sets.

Also, as these images are from the whole head, only a specific part of the image is usefull for this classification, we performed different preprocessing before feeding then to the DL input. In a preprocessing step, each original image is first cropped to the interesting part (Test1: size 488x488), then resized to (Test2: 244x244) or (Test3: 64x64) and after resizing to 244x244, they are Sobel filtered to enhance the contours of the image (Test 4). Figure 2 shows an example of these inputs.

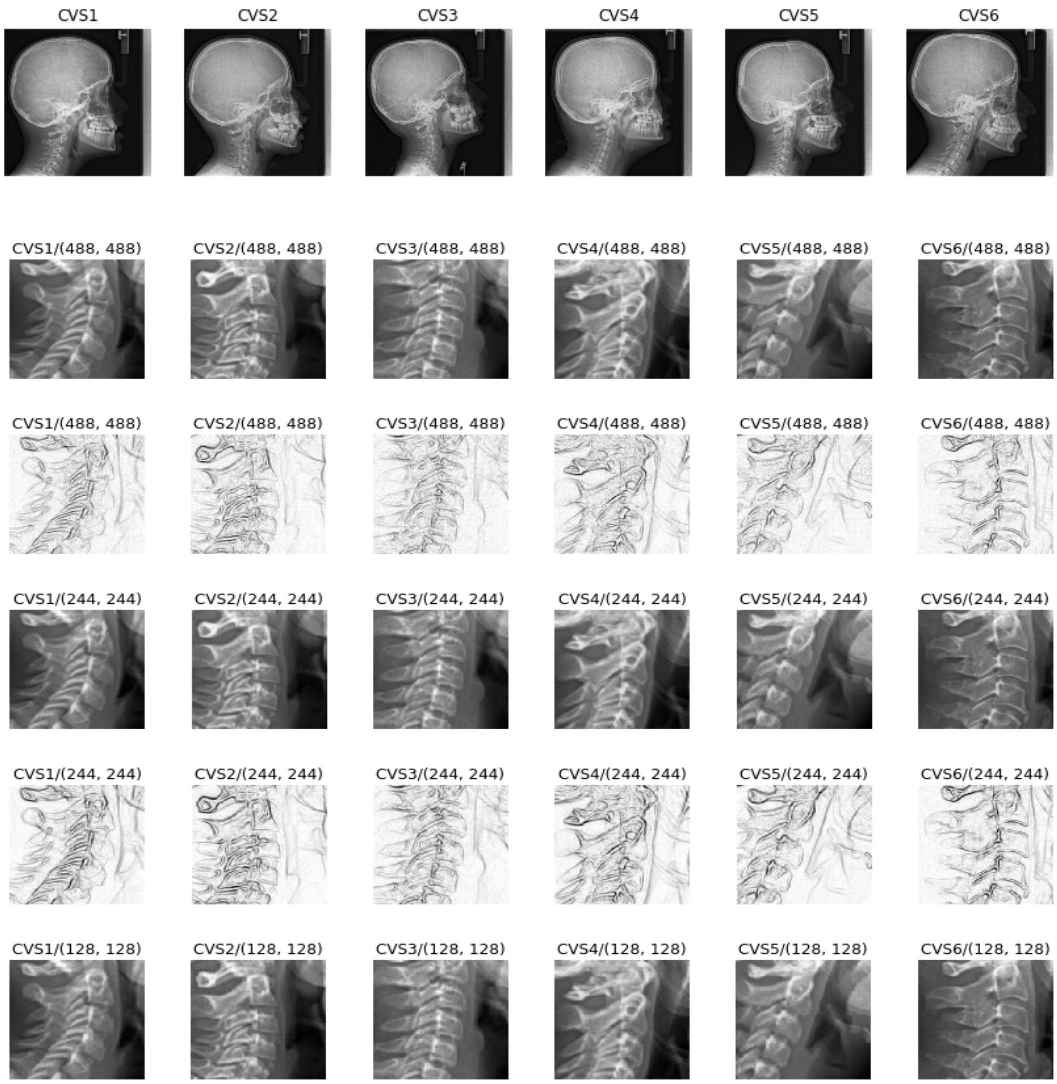

Figure 2. Originals and different preprocessing before training: a) Originals (2012x2020), b) test0: cropped images (488x488), c) test1: cropped and sobel edge detector filter (488x488), d) test2: cropped and resized (244x244), e) test3: cropped, resized and sobel edge detector filter (244x244), f) test4: cropped and resized (64x64)

3. Structure of the Deep Learning network

In a preliminary study, we used different Deep Learning network structures for this classification task and finally we selected a Deep Learning structure (like resnet) which is adapted for our task.

We considered different classical networks:

- Resnet :
  Resnet was introduced in the paper "Deep Residual Learning for Image Recognition <https://arxiv.org/abs/1512.03385>". There are several variants with different output sizes, including Resnet18, Resnet34, Resnet50, Resnet101, and Resnet152, all of which are available from torchvision models. As our dataset is small, we used Resnet18 that we adapted in our case for 6 classes.
- Alexnet:
  Alexnet was introduced in the paper "ImageNet Classification with Deep Convolutional Neural Networks
  <https://papers.nips.cc/paper/4824-imagenet-classification-with-deep-convolutional-neural-networks.pdf> and was the first very successful CNN on the ImageNet dataset.
- VGG:
  VGG was introduced in the paper "Very Deep Convolutional Networks for Large-Scale Image Recognition <https://arxiv.org/pdf/1409.1556.pdf>". Torchvision offers eight versions of VGG with various lengths and some that have batch normalizations layers.
- Squeezenet:
  The Squeeznet architecture is described in the paper "SqueezeNet: AlexNet-level accuracy with 50x fewer parameters and <0.5MB model size", <https://arxiv.org/abs/1602.07360>". It uses a different output structure than the other models mentioned here. Torchvision has two versions of Squeezenet. We used version 1.0.
- Densenet:
  Densenet was introduced in the paper "Densely Connected Convolutional Networks", <https://arxiv.org/abs/1608.06993>. Torchvision has four variants of Densenet. Here we used Densenet-121 and modified the output layer, which is a linear layer with 1024 input features, for our case.
- Inception v3:
  Inception v3 was first described in "Rethinking the Inception Architecture for Computer Vision", <https://arxiv.org/pdf/1512.00567v1.pdf>. This network is unique because it has two output layers when training. The second output is known as an auxiliary output and is contained in the AuxLogits part of the network. The primary output is a linear layer at the end of the network. Note, when testing we only consider the primary output.

As it can be seen from on Figure 3, the structure of Deep Learning model is composed of an input convolutional layer and three or four other convolutional nets (CNN) layers and a fully connected of (32x32) to 6 classes. Each of the three CNNs is followed by a normalization, pooling and dropout layers with different dropout coefficients.

The models are trained with different partitions of the images in Training, Validation and Testing sets. The following figure shows 300 images which have been prepared for the training, then validated on 200 images and saved to be used for testing step. A set of 120 images are used for testing step and the average score was 80 percent.

4. Tools and Implementation

In this work, we used the following tools:

- SciKit-Learn: Data shuffling, Kmeans and Gaussian Mixture clustering, Principal Component Analysis and performance metrics.
- Keras wth tensorflow backend: VGG16, VGG19 and ResNet50 convolution network models with ImageNet weights

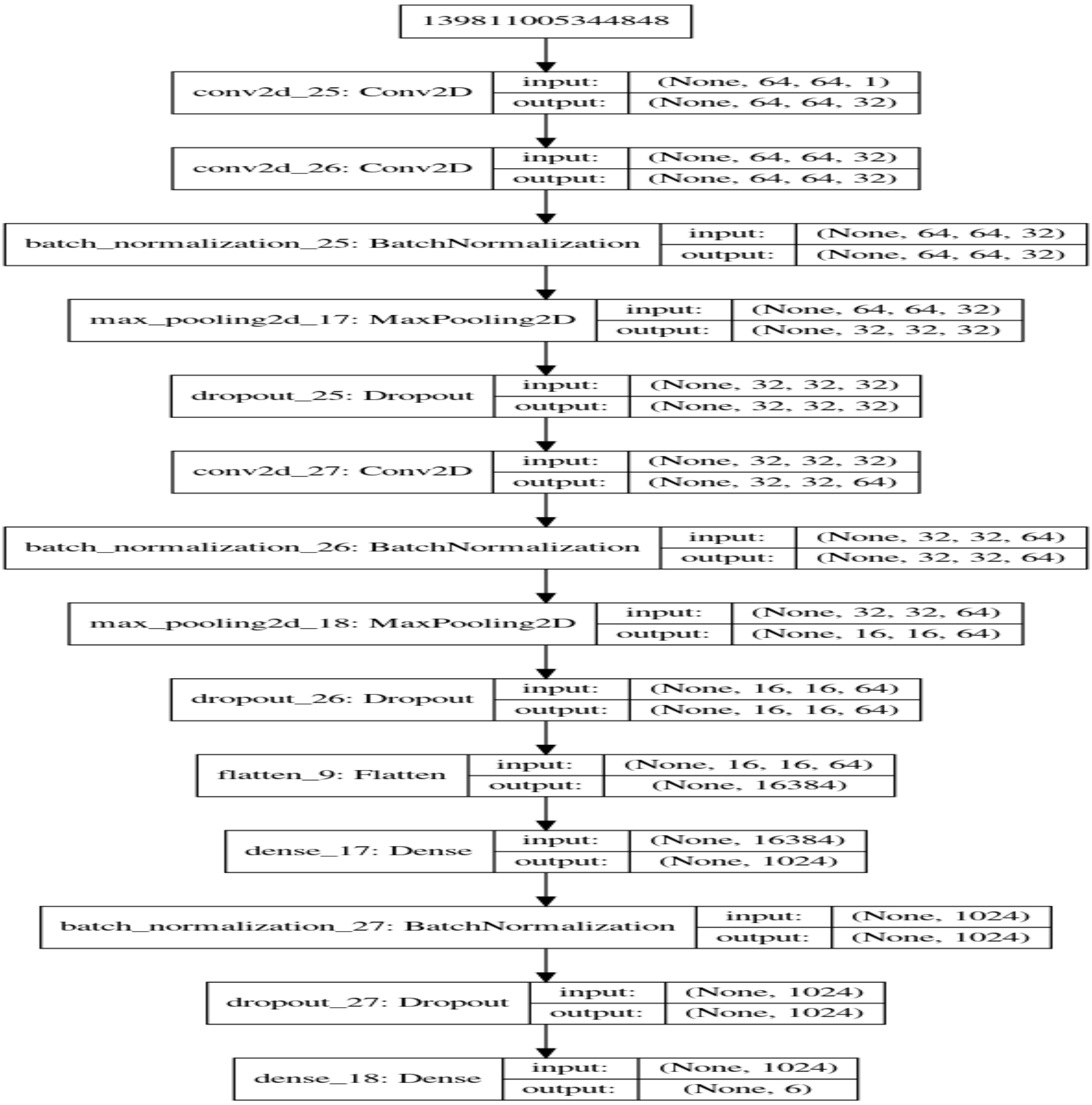

Figure 3. The structure of the proposed Deep Learning network

5. Prediction results

With implemented DL structure, we used 300 images for the training step, 200 images for the validation step and finally 150 images for the testing step. We had to fix a great number of parameters such as dropout rates, optimization algorithms, regularization parameters, etc.

The following figure shows the evolution of the Loss function and the accuracy as a function of the epoch numbers for one of these different tests.

Here, we show the prediction results obtained with different preprocessing of the data, both during the training and the testing

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CVS1/ 0.83,  CVS2/ 0.85,  CVS3/ 0.72,  CVS4/ 0.72,  CVS5/ 0.79,  CVS6/ 0.82
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6. Conclusions

In this work, we developed and presented a specifically designed classification method for classifying the lateral radiographs of a great number of patients with the objective of determining the cervical vertebra maturation degree of bones, which is an important parameter for the orthodontists.

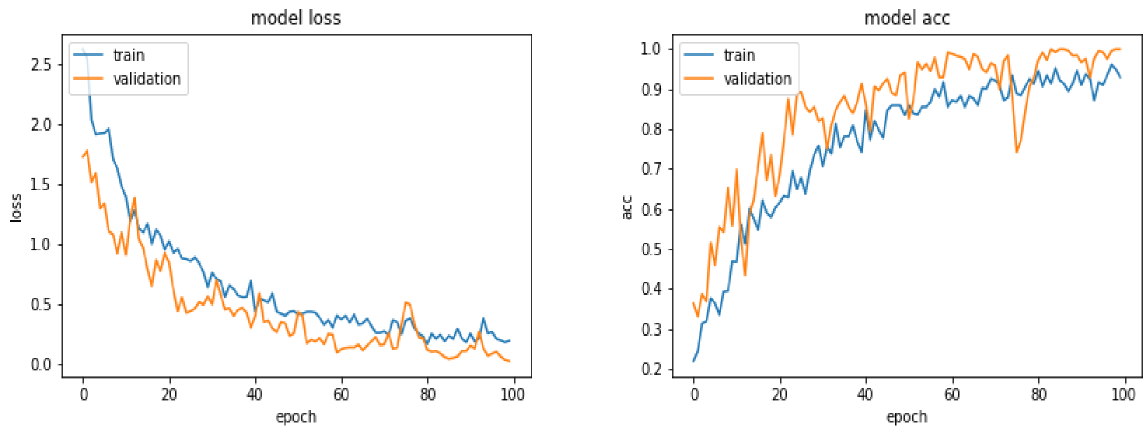

Figure 4. Evolution of the Loss function and the accuracy as a function of the epoch numbers.

The proposed Deep Learning classification method is particularly adapted for this task. In a first step, we used 300 labeled images for training, 200 for validation and hyper parameter tuning and finally 100 for testing. Even if during the training and validation, we could obtain accuracies more than 95%, the accuracy for the testing images did not exceeded 85%. We think that with a greater number of training and validation images, this can be improved. Our plan is to use about 1000 images for training and 1000 for testing in near future.

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