

End-to-end learning for semiquantitative rating of COVID-19 severity on Chest X-rays

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Abstract

In this work we design an end-to-end deep learning architecture for predicting, on Chest X-rays images (CXR), a multi-regional score conveying the degree of lung compromise in COVID-19 patients. Such semi-quantitative scoring system, namely **Brixia score**, is applied in serial monitoring of such patients, showing significant prognostic value, in one of the hospitals that experienced one of the highest pandemic peaks in Italy. To solve such a challenging visual task, we adopt a weakly supervised learning strategy structured to handle different tasks (segmentation, spatial alignment, and score estimation) trained with a “from part to whole” procedure involving different datasets. In particular, we exploit a clinical dataset of almost 5,000 CXR annotated images collected in the same hospital. Our BS-Net demonstrates self-attentive behavior and a high degree of accuracy in all processing stages. Through inter-rater agreement tests and a gold standard comparison, we show that our solution outperforms single human annotators in rating accuracy and consistency, thus supporting the possibility of using this tool in contexts of computer-assisted monitoring. Highly resolved (super-pixel level) explainability maps are also generated, with an original technique, to visually help the understanding of the network activity on the lung areas. We also consider other scores proposed in literature and provide a comparison with a recently proposed non-specific approach. We eventually test the performance robustness of our model on a variegated public COVID-19 dataset, for which we also provide **Brixia score** annotations, observing good direct generalization and fine-tuning capabilities that highlight the portability of BS-Net in other clinical settings. The CXR dataset along with the source code and the trained model are publicly released for research purposes.

Keywords: COVID-19 severity assessment, Chest X-Rays, semi-quantitative rating, End-to-end learning, Convolutional Neural Networks

1. Introduction

Worldwide, the saturation of healthcare facilities, due to the high contagiousness of Sars-Cov-2 virus and the significant rate of respiratory complications (WHO,

2020), is indeed one among the most critical aspects of the ongoing COVID-19 pandemic. As we write, in many countries virulence has not yet peaked, while in others a second wave is feared. Under these conditions, it is extremely important to adopt all types of measures to improve the accuracy in monitoring the evolution of the disease and the level of coordination and communication between different clinicians for the streamlining of health-care procedures, from facility- to single patient-level. In this context, thoracic imaging, specifically chest X-ray

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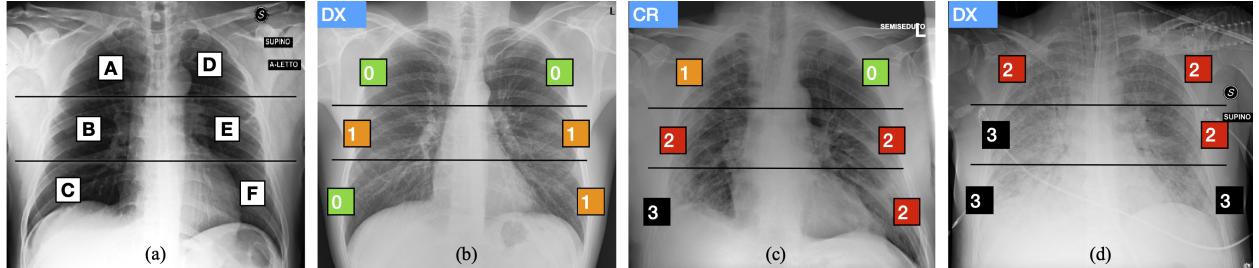


Figure 1. Brixia score: (a) zone definition and (b-d) examples of annotations. Lungs are first divided into six zones on frontal chest radiograph. Line A is drawn at the level of the inferior wall of the aortic arch. Line B is drawn at the level of the inferior wall of the right inferior pulmonary vein. A and D upper zones; B and E middle zones; C and F lower zones. A score ranging from 0 (green) to 3 (black) is then assigned to each sector, based on the observed lung abnormalities.

(CXR) and computed tomography (CT), are playing an essential role in the management of patients, especially those evidencing risk factors (from triage phases) or moderate to severe COVID-19 signs of pulmonary disease (Rubin et al., 2020). In particular, CXR is a widespread, relatively cheap, fast, and accessible diagnostic modality, which may be easily brought to the patient's bed, even in the emergency departments. Therefore, the use of CXR may be preferred to CT not only in limited resources environments, but where this becomes fundamental to avoid handling of more compromised patients, or to prevent infection spread due to patient movements from and towards radiology facilities (Manna et al., 2020). Moreover a serious X-ray dose concern arises in this context, where serial image acquisitions on a daily basis are often advisable due to the frequency of rapid worsening of the disease and the need of a prompt assessment of the therapy effects. For these reasons, notwithstanding a lower sensitivity compared to CT, CXR has been set up as a first diagnostic imaging option for COVID-19 severity assessment and disease monitoring in many healthcare facilities.

Due to the projective nature of the CXR image and the wide range of possible disease manifestations, a precise visual assessment of the entity and severity of the pulmonary involvement is particularly challenging and semi-quantitative scoring systems are usually adopted to map radiologist judgments to numerical scales. This leads to a more objective reporting and improved communication among specialists. In particular, from the beginning of the pandemic phase in Italy, the Radiology Unit 2 of ASST Spedali Civili di Brescia introduced a multi-valued scor-

ing system, namely **Brixia score**, that was immediately implemented in the clinical routine (Borghesi and Maroldi, 2020). With this system, the lungs are divided into six regions, and the referring radiologist assigns to each region an integer rating from 0 to 3, based on the local assessed severity of lung compromise (see Figure 1 and Section 3.1 for details). Other scores have been recently proposed as well, which are less resolute either in terms of intensity scale granularity (Toussie et al., 2020), or localization capacity (Wong et al., 2020; Cohen et al., 2020a) (see Section 3.2). Severity scores offer a mean to introduce the use of representation learning techniques to automatically assess disease severity using artificial intelligence (AI) approaches starting from CXR analysis. However, while in general computer-aided interpretation of radiological images based on Deep Learning (DL) can be an important asset for a more effective handling of the pandemic in many directions (Shi et al., 2020), the early availability of public datasets of CXR images from COVID-19 subjects catalyzed the research almost exclusively on assisted COVID-19 diagnosis (i.e. dichotomous or differential diagnosis versus other bacterial/viral forms of pneumonia). This happened despite the fact that normal CXRs do not exclude the possibility of COVID-19, and abnormal CXR is not enough specific for a reliable diagnosis (Rubin et al., 2020). Moreover, much research applying AI to CXR in the context of COVID-19 diagnosis considered small or private datasets, or lacked rigorous experimental methods, potentially leading to overfitting and performance overestimation (Castiglioni et al., 2020; Maguolo and Nanni, 2020; Tartaglione et al., 2020).

So far, no much work has been done in other directions, such as COVID-19 severity assessment from CXR, despite this has been highlighted as one of the highest reasonable research efforts to be pursued in the field of AI-driven COVID-19 radiology (Laghi, 2020; Cohen et al., 2020c).

1.1. Aims and contributions

Main goal. In this work, we aim at introducing the first representation-learning solution specifically designed to obtain an effective and reliable assessment of the severity of COVID-19 disease by means of an automated CXR interpretation. This system must be able to produce a multi-regional scoring estimation by autonomously operating on data directly coming from different X-ray modalities (computed radiography, CR, and digital radiography by Direct X-ray detection, DX), acquisition directions (anteroposterior, AP, and posteroanterior, PA) and patient conditions (e.g., standing, supine, with or w/o the presence of life support systems), providing robust data conditioning and self-attentive behavior. This corresponds to a highly difficult visual task, as further detailed in Section 3.

Large CXR database. For this purpose, we collected and operated on a large dataset of almost 5,000 CXRs, which can be assumed representative of all possible manifestations and degrees of severity of the COVID-19 pneumonia, since these images come from the whole flow of hospitalized patients in one of the biggest health facilities in northern-Italy during the pandemic peak. Since a highly-expressive multi-zone scoring system (**Brixia score**) was adopted from the very beginning of the pandemic period, our CXR dataset is fully annotated with scores directly coming from the patients' medical records, as provided by the reporting radiologist on duty among the about 30 specialists forming the radiology staff. Therefore, we have the possibility to work on a complete and faithful picture of an intense and emergency-driven clinical activity.

Weakly supervised learning framework. Given the difficulties and pitfalls in the visual interpretation of the disease signs on CXRs (spanning from subtle findings to heavy lung impairment), the lack of detailed localization information, and the unavoidable inter-rater variability in the semi-quantitative scoring, we was compelled to operate in a weakly supervised learning framework (Zhou,

2017). Far from constituting in itself a “weakness”, these approaches have demonstrated to be highly valuable methods to leverage available knowledge in medical domains (Xu et al., 2014; Wang et al., 2017; Karimi et al., 2019; Bontempi et al., 2020; Tajbakhsh et al., 2020). All this given, and being the adopted scoring system the richer among others proposed for the same purpose (see Sec. 3.2), our goal results to be particularly challenging, especially considering radiologists' performance as a target to reach, and to possibly overcome.

End-to-end severity assessment architecture. We developed an original *multi-network* Deep Learning-based architecture of which we give a high-level representation in Figure 2. The system is designed as to learn and execute different tasks such as: data normalization, lung segmentation, geometric alignment, feature extraction, and the final multi-valued score estimation. Although the presence of specific task dedicated stages, the overall logic is *end-to-end*, which is reached through a hierarchical organization of the training, according to a *from-the-part-to-the-whole* strategy. This consists of leveraging multiple datasets of various nature and origins (described in Section 4) for early training stages, then arriving at a global (involving all network portions) severity assessment training, based on the large collected dataset. Our end-to-end network architecture, called BS-Net and described in detail in Section 5, is thus characterized by the joint work of different sections, represented as a group of four hexagons in Figure 2, comprising 1) a shared multiresolution feature extraction backbone, 2) a state-of-art lung segmentation branch, 3) an original registration mechanism capable of spatially normalizing the feature computation stream in the backbone, and 4) a multi-regional classification part for the final six-valued score estimation. Performance robustness is also guaranteed by the choice of the loss function which comprises a differentiable version of the target discrete metric.

Explainability maps. In the perspective of a responsible and transparent exploitation of the proposed solution, there is the need to establish a communication channel between the specialist and the AI system. Given the spatial distribution of the severity assessment we need highly resolved explainability maps. To this end we propose an original technique (described in Section 5.4) able to create highly structured explanation maps at a superpixel level.

Experimental goals. A complete set of Results (Sec-

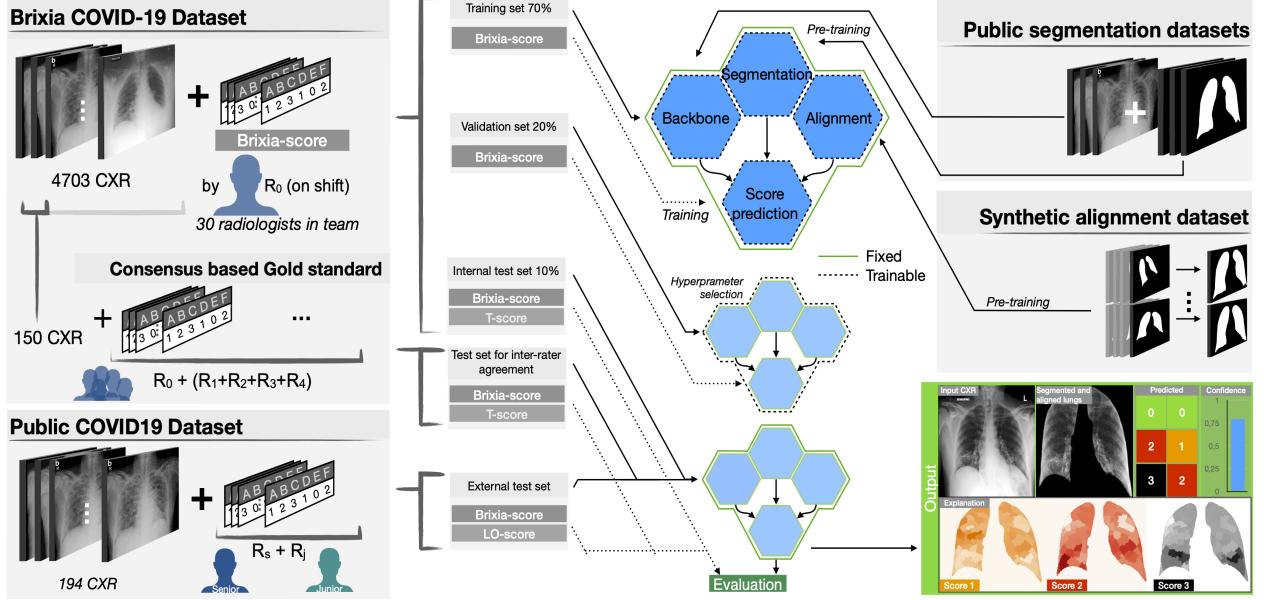


Figure 2. Overview of the proposed method.

tion 6) and related Discussion (Section 7) are articulated in a multi-purpose validation path. 1) In terms of system performance assessment, we select optimal configurations and justify architectural choices also considering different possible alternatives from the literature. 2) To cope with the inter-rater variability and to demonstrate above radiologists' performance, we involve a team of specialists to establish a consensus-based gold-standard as a reference for both single radiologist and our model ratings. 3) We consider other scores proposed in the literature and provide a comparison with a recently proposed non-specific approach for demonstrating both system versatility and performance boost coming from the adoption of a specifically designed solution to severity assessment. 4) We address the problem of portability of the proposed solution on CXRs coming from different worldwide contexts by providing new annotations and assessing our system behavior on a public CXR dataset of reference for COVID-19.

Data, Code, and Model distribution. The whole dataset along with the source code and the trained model are available from <http://github.org/BrixIA>.

2. Related Work

Since the very beginning of the pandemic, the attention and resources of researchers in digital technologies (Ting et al., 2020), AI and data science (Latif et al., 2020) have been captured by COVID-19. A review of artificial intelligence techniques in imaging data acquisition, segmentation, and diagnosis for COVID-19 has been made in Shi et al. (2020), where authors structured previous work according to different tasks, e.g., contactless imaging workflow, image segmentation, disease detection, radiomic feature extraction, etc.

The use of convolutional neural networks (CNN) to analyze CXRs for presumptive early diagnosis and better patient handling based on signs of pneumonia, has been proposed by (Oh et al., 2020) at the very beginning of the outbreak, when a systematic collection of a large CXR dataset for deep neural network training was still problematic. As the epidemic was spreading, the increasing availability of CXR datasets from patients diagnosed with COVID-19 has polarized almost all the research efforts on diagnosis-oriented image interpretation studies. As it is hard to mention them all (we counted more than 80 studies, most of them in a pre-print format), the reader

can refer to an early reviewing effort Shi et al. (2020), while here we derive the most relevant emerging issues. Most methods exploit available public COVID-19 CXR datasets (Kalkreuth and Kaufmann, 2020). Constantly updated collections of COVID-19 CXR images are curated by the authors of (Linda Wang and Wong, 2020)² and (Cohen et al., 2020b)³. Prior to COVID-19, large CXR datasets have been released and also used in the context of open challenges for the analysis of different types of pneumonia Wang et al. (2017)⁴ or pulmonary and cardiac (cardiomegaly) diseases Irvin et al. (2019)⁵. These datasets are usually exploited as well in works related to COVID-19 diagnosis, as in (Minaee et al., 2020), to pre-train existing networks and fine-tune them on a reduced set of COVID-19 CXRs, or to complete case categories when the focus is on differential diagnosis to distinguish from other types of pneumonia (Linda Wang and Wong, 2020; Oh et al., 2020; Li et al., 2020b). However, beyond the fact that CXR modality should be more appropriate for patient monitoring and severity assessment than for primary COVID-19 detection, other issues severely affect the previous studies which employed CXR for COVID-19 diagnosis purposes (Burlacu et al., 2020). In particular, many of these data-driven works are interesting in principle, but almost all would require and benefit from extensions and validation on a higher number of CXRs from COVID-19 subjects. Working with datasets of a few hundred images, when analyzed with deep architectures, often results in severe overfitting and can encounter issues generated by unbalanced classes when larger datasets are used to represent other kinds of pneumonia (Pereira et al., 2020). Moreover, most of the studies issued in this emergency period are often based on sub-optimal experimental designs, and the numerous still unknowns factors about COVID-19 severely undermine the external validity and generalizability of the performance of diagnostic tests (Sardanelli and Di Leo, 2020). In (Maguolo and Nanni, 2020) it is pointed out that many CXR based systems seem to learn to recognize more the character-

istics of the dataset rather than those related to COVID-19. This effect can be overcome, or at least mitigated, by working on more homogeneous and larger datasets, as in (Castiglioni et al., 2020), or by preprocessing the data as in (Pereira et al., 2020). In addition, automated lung segmentation can play an essential role in the design of a robust respiratory disease interpretation system, either diagnosis-oriented (Tartaglione et al., 2020) or, as we see in this work, for pneumonia severity assessment. Lung segmentation on CXR has been recently witnessing a convergence towards encoder-decoder architectures, such as in the U-Net framework (Ronneberger et al., 2015), and in the fully convolutional approach found in Long et al. (2015). All these approaches share skip connections as a common key element, originally found in ResNet (He et al., 2016) and DenseNet architectures (Huang et al., 2017). The idea behind skip connections is to combine coarse-to-fine activation maps from the encoder within the decoding flow. In doing so, these models are capable of efficiently using the extracted information from different abstraction layers. In Zhou et al. (2018), a nested U-Net is presented, bringing the idea of skip connection to its extreme. This approach is well suited to capture fine-grained details from the encoder network, and exploding them in the decoding branch. Last, in critical sectors like healthcare, the lack of understanding of complex machine-learned models is hugely problematic. Therefore, explainable AI approaches able to reveal to physicians where is directed the model attention (Karim et al., 2020; Oh et al., 2020; Rajaraman et al., 2020; Reyes et al., 2020), are always desirable. Despite some evidenced issues, there is still an abundant ongoing effort on AI-driven approaches for COVID-19 detection based on CXR analysis. However, in the global race to contain and treat COVID-19 (Kundu et al., 2020), AI-based solutions have high potentials to expand the role of chest imaging beyond diagnosis, to facilitate risk stratification, disease progression monitoring, and trial of novel therapeutic targets. Cautions about a radiologic diagnosis of COVID-19 infection driven by deep learning have been also expressed by Laghi (2020), who states that a more interesting application of AI in COVID-19 infection is to provide for a more objective quantification of the disease, in order to allow the monitoring of the prognostic factors (i.e., lung compromising severity) for appropriate and timely patient treatment. For example, the presence of AI-assisted first

²<https://github.com/lindawangg/COVID-Net/blob/master/docs/COVIDx.md>

³<https://github.com/ieee8023/covid-chestxray-dataset>

⁴<https://www.kaggle.com/c/rsna-pneumonia-detection-challenge/data>

⁵<https://stanfordmlgroup.github.io/competitions/chexpert/>

preliminary readings, or working with AI-generated second opinions, can lead to better procedures in terms of speed-up and efficiency of decision-making, especially in critical conditions like the ones characterizing the management of health facilities overload. In particular, we did not find dedicated AI-driven solutions for disease monitoring and lung severity assessment based on CXR, although this modality, for the aforementioned reasons, is part of the routine practice in many institutions, like the one from which this study originates. In (Cohen et al., 2020a), different kinds of features coming from a neural network pre-trained on non-COVID-19 CXR datasets are considered in their predictive value on the estimation of COVID-19 severity scores. In (Li et al., 2020a) a good correlation is reported between a lung based severity score judgement and machine prediction by using a transfer learning approach from a large non-COVID-19 dataset to a small COVID-19 one. However, authors acknowledge several limitations in the capability to handle image variability that can arise due to patient condition and image acquisition settings.

From these early studies, the need for dedicated research toward solutions for the challenging visual task of COVID-19 severity assessment on CXRs coming from real clinical settings, and the necessity to operate on large annotated datasets, clearly emerge.

3. Scoring systems for severity assessment

CXR severity scoring based on the subdivision of lungs in different regions (Borghesi and Maroldi, 2020; Toussie et al., 2020; Wong et al., 2020) evidenced significant prognostic value when applied in serial monitoring of COVID-19 patients (Borghesi et al., 2020a,b). Since the radiologists are asked to map a global or region-based qualitative judgment on a quantitative scale, this diagnostic image interpretation task can be defined as *semi-quantitative*, i.e. characterized by a certain degree of subjectivity. Following, a detailed description of the three semi-quantitative scoring systems we found in use and we also consider in this work.

3.1. Brixia score

The multi-region and multi-valued Brixia score was designed and implemented in routine reporting by the Ra-

diology Unit 2 of ASST Spedali Civili di Brescia (Borghesi and Maroldi, 2020), and later validated for risk stratification on a large population in (Borghesi et al., 2020b). According to it, lungs in antero-posterior (AP) or postero-anterior (PA) views, are subdivided into six zones, three for each lung, as shown in Figure 1(a). For each zone, a score 0 (no lung abnormalities), 1 (interstitial infiltrates), 2 (interstitial and alveolar infiltrates, interstitial dominant), or 3 (interstitial and alveolar infiltrates, alveolar dominant) is assigned, based on the characteristics and extent of lung abnormalities. The six scores can be aggregated to obtain a Global Score in the range [0, 18]. Examples of scores assigned to different cases are showcased in Figure 1(b-d). As in daily practice CXR exams are inevitably reported by different radiologists, this combined codification of the site and type of lung lesions makes the comparison of CXR exams faster and significantly more consistent, and this allows a better handling of patients.

3.2. Other severity scores and possible relations among them

In (Toussie et al., 2020) the presence/absence of pulmonary COVID-19 alterations is mapped on a 1/0 score associated to each of six pulmonary regions according to a subdivision scheme substantially reproducing the one of the Brixia score. We here refer to this score as T score which globally ranges from 0 to 6. By ignoring slight differences in terms of anatomic landmarks that guide the radiologist to determine the longitudinal lung subdivisions, the T score can be directly estimated from the Brixia score by just mapping the set of values {1, 2, 3} of the latter to the value 1 of the former.

In (Cohen et al., 2020a) two different COVID-19 severity scores are considered which are derived and simplified versions of a composite scoring system proposed by (Warren et al., 2018) in the context of lung oedema. Both scores are composed by couples of values, one for each lung: 1) a geographic extent score, here GE score, in the integer range [0, 8] and 2) a lung opacity score, here LO score in the integer range [0, 6]. The GE score, introduced in (Wong et al., 2020) for COVID-19 severity assessment, assigns for each lung a value depending on the extent of involvement by consolidation or ground glass opacity (0 = no involvement; 1 ≤ 25%; 2 = 25–50%; 3 = 50–75%; 4 ≥ 75% involvement). While this area-based

quantification has no clear correspondence to the judgment made with the **Brixia score**, a possible mapping can be estimated with the **LO score** (e.g., by a simple linear regression, as we will see in Sec.6.5), which assigns for each lung a value depending on degree of opacity (0 = no opacity; 1 = ground glass opacity; 2 = consolidation; 3 = white-out). A global score derived by a modified version of the ones introduced in (Warren et al., 2018) has been also used in (Li et al., 2020a).

3.3. AI-based prediction of severity scores

At first sight, an automatic assessment of a semi-quantitative prognostic score may seem easier than other tasks, such as differential diagnosis, or purely quantitative severity evaluations. Nevertheless, when dealing with semi-quantitative scores, major critical aspects arise.

First, the difficulty of establishing a ground truth information, since subjective differences in scoring are expressed by different radiologists while assessing and qualifying the presence of, sometimes subtle, abnormalities. This differs from more quantitative tasks that can be associated to measurable targets, as in the case of DL-based quantitative (volumetric) measure of opacities and consolidations on CT scans for lung involvement assessment in COVID-19 pneumonia (Huang et al., 2020; Gozes et al., 2020; Lessmann et al., 2020). The application of quantitative methods to AI-driven assessment of COVID-19 severity on CXR, however, is not advisable due to the projective nature of these images, with inherent ambiguities in relating opacity area measures to corresponding volumes.

A semi-quantitative scoring system can instead leverage the sensitivity of CXR as well as the ability of radiologists to detect COVID-19 pneumonia and communicate in an effective way its severity according to an agreed severity scale.

Second, the exact localization of the lung zones and of severity-related findings (even within each of the selected lung zones) remains implicit and related to the visual attention of the specialist in following anatomical landmarks (without any explicit localization information indicated with the score, nor any lung segmentation provided). This results in the difficulty to define reference spatial information usable as ground truth and implies significantly incomplete annotations with respect to the task.

Eventually, the same visual task related to global or localized COVID-19 severity assessment is challenging in itself, since CXR findings may be extremely variable (from no or subtle signs to extensive changes that modify anatomical patterns and borders), and the quality of the information conveyed by the images may be impaired from the presence of medical devices, or from sub-optimal patient positioning.

All these factors, if not handled, can impact in an unpredictable way on the reliability of an AI-based interpretation. This concomitant presence of quantitative and qualitative aspects, on a difficult visual analysis task, makes the six-valued **Brixia score** estimation on CXR particularly challenging.

4. Dataset

Training and validation of the proposed multi-network architecture (Figure 2) require the use of multiple datasets, which are described in the following.

4.1. Segmentation datasets

For the segmentation module we exploit and merge three different datasets: Montgomery County (Jaeger et al., 2014), Shenzhen Hospital (Stirenko et al., 2018), and JSRT databases (Shiraishi et al., 2000), for a total of about 1,000 images. When indicated we adopt the original training/test set splitting (as for the JSRT database); otherwise, we consider the first 50 images as test set, and the remaining as training set (see Table 1).

Table 1
Segmentation datasets.

	Training-set	Test-set	Split
Montgomery County	88	50	first 50
Shenzhen Hospital	516	50	first 50
JSRT database	124	123	original
Total	728	223	

4.2. Alignment dataset

CXRs acquired in a real clinical setting lack of standardized levels of magnification and alignment of the lungs. Moreover, possible patient positions are different

(standing, sitting, prone, supine) and, according to subject conditions, it is not always feasible to produce images with an ideal shooting of the chest. To avoid the inclusion of anatomical parts not belonging to the lungs in the AI pipeline, which would increase the task complexity and introduce unwanted biases, we integrate in the pipeline an alignment block. This exploits the same images used for the segmentation stage to create a synthetic dataset formed by artificially transformed images (see Table 2), including random rotations, shifts, and zooms, which are used in first phases of the training, in an on-line augmentation fashion, using the framework provided in (Buslaev et al., 2020).

Table 2

Alignment dataset: synthetic transformations. The parameters refer to the implementation in Albumentation (Buslaev et al., 2020). In the last column is expressed the probability of application of each transformation.

	Parameters (up to)	Probability
Rotation	25 degree	0.8
Scale	10%	0.8
Shift	10%	0.8
Elastic transformation	alpha=60, sigma=12	0.2
Grid distortion	step=5, limit=0.3	0.2
Optical distortion	distort=0.2, shift=0.05	0.2

4.3. Brixia COVID-19 dataset

We collected a large dataset of CXR images corresponding to the entire amount of images taken for both triage and patient monitoring in sub-intensive and intensive care units during one month (between March 4th and April 4th 2020) of pandemic peak at the ASST Spedali Civili di Brescia, and contains all the variability originating from a real clinical scenario. It includes 4,707 CXR images of COVID-19 subjects, acquired with both CR and DX modalities, in AP or PA projection, and retrieved from the facility RIS-PACS system. All data are directly imported from DICOM files, consisting in 12-bit gray-scale images, and mapped to float32 between 0 and 1. To mitigate the grayscale variability in the dataset, we normalize the appearance of the CXR by sequentially applying an adaptive histogram equalization (CLAHE, clip:0.01), a median filtering to cope with noise (kernel size: 3), and a clipping outside the 2nd and 98th percentile.

All image reports include the Brixia score as a string of six digits indicating the scores assigned to each region. The Global Score is simply the sum of the six numbers. Each image has been annotated with the six-valued score by the radiologist on shift (here referred to as R_0), belonging to a team of about 30 radiologists operating in different radiology units of the hospital with a very wide range of years of experience and different specific expertise in imaging of the chest. All images were collected and anonymized, and their usage for this study had the approval of the local Ethical Committee (#NP4121) that also granted an authorization to release the whole anonymized dataset for research purposes. The main characteristics of the dataset are summarised in Table 3.

Table 3
Brixia COVID-19 dataset details.

Parameter	Value
Modality	CR (62%) - DX (38%)
View position	AP (87%) - PA (13%)
Manufacturers	Carestream, Siemens
Image size	$(1056 \div 3050) \times (1186 \div 3376)$
No. of images	4,703
Training set	3,311 images
Validation set	945 images
Test set	447 images

4.3.1. Consensus-based Gold Standard

To assess the level of inter-rater agreement among human annotators, we asked other 4 radiologists to rate a subset of 150 images belonging to the test set of the Brixia COVID-19 dataset. While R_0 is the original clinical annotation in the patient report, we name R_1, R_2, R_3 , and R_4 the four radiologists that provided additional scores. Their expertise is variegated so as to represent the whole staff experience: we have one resident at the 2nd year of training, and three staff radiologists with 9, 15 and 22 years of experience (reported numerical ordering of R_i does not necessarily correspond to seniority order). A Gold

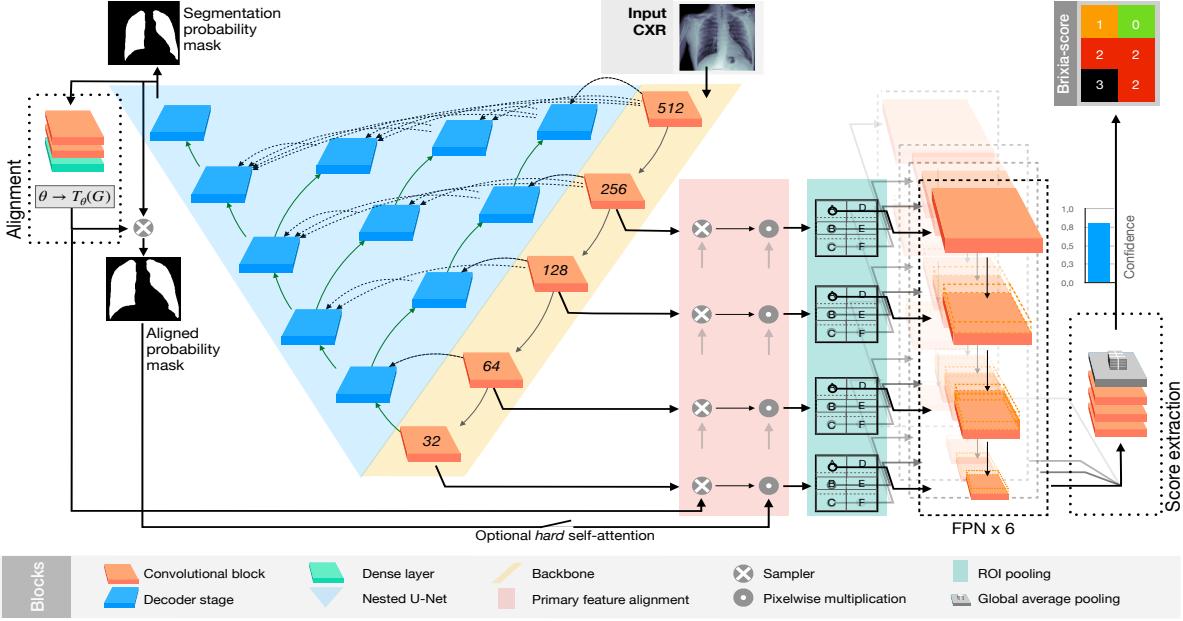


Figure 3. Detailed scheme of the proposed architecture. In particular, in the top-middle the CXR to be analyzed is fed to the network. The produced outputs are: the segmentation mask of the lungs (top-left); the aligned mask (middle-left); the Brixia score (top-right).

Standard score is then built based on a majority criterion, by exploiting the availability of multiple ratings (by R_0, R_1, R_2, R_3 , and R_4), using seniority in case of equally voted scores. Building such Gold Standard is useful, on the one hand, to grasp the inbuilt level of error in the training set, and on the other hand, to gain a reference measure for human performance and inter-rater variability assessments.

4.4. Public COVID-19 dataset

To later demonstrate the robustness and the portability of the proposed solution, we exploit the public repository by Cohen et al. (2020b), which contains CXR images of patients which are positive or suspected of COVID-19⁶. This dataset is an aggregation of CXR images collected in several centers worldwide, at various spatial resolutions, and other unknown image quality parameters, such as modality and window-level settings. In order to contribute to such public dataset, two expert radiologists, a board-

certified staff member R_s and a trainee R_j , with 22 and 2 years of experience, respectively, produced the related Brixia score annotations for CXR in this collection, exploiting Labelbox⁷, an online solution for labelling. After discarding problematic cases (e.g., images with a significant portion missing, too low resolution/quality, the impossibility of scoring for external reasons, etc.), the obtained dataset is composed of 192 CXRs, completely annotated according to the Brixia score system⁸.

5. End-to-end multi-network model

5.1. Proposed architecture

To predict the pneumonia severity of a given CXR, we propose a novel architecture where different networks co-operate, in an end-to-end scheme, to segment, align, and predict the Brixia score. The global scheme is depicted in Figure 3, while details on single parts follow.

⁷<https://labelbox.com/>

⁸Available from both <https://github.com/BrixIA/Brixia-score-COVID-19> and <https://github.com/ieee8023/covid-chestxray-dataset>

Backbone. The input image is initially processed by a cascade of convolutional blocks, referred to as Backbone (in yellow in Figure 3). This cascade is used both as the encoder section of the segmentation network, and as the feature extractor for the Feature Pyramid Network of the classification branch. To identify the best solution at this stage, we tested different backbones among the state-of-the-art, i.e., ResNet (He et al., 2016), VGG (Simonyan and Zisserman, 2014), DenseNet (Huang et al., 2017), and Inception (Szegedy et al., 2017).

Segmentation. Lung segmentation is performed by a nested version of U-net, also called U-Net++ (Zhou et al., 2018), a specialized architecture oriented to medical image segmentation (in blue in Figure 3). It is composed of an encoder-decoder structure, where the encoder branch (i.e., the Backbone) exploits a nested interconnection to the decoder.

Alignment. The segmentation probability map in output is then used to estimate the alignment transformation, which is employed to align both the segmentation mask and the feature pyramid. Alignment is achieved through a spatial transformer network (Jaderberg et al., 2015) able to estimate the spatial transform matrix to center and correctly zoom the lungs. This alignment block, pre-trained on the synthetic alignment dataset, produces a self-attentive mechanism useful to propagate the correct area of the lungs, through the ROI (Region Of Interest) pooling, towards the final classification stage. In Figure 4 a high-level representation where the alignment through resampling is depicted on the left. This resampling scheme can be used for both the features from the backbone and for the segmentation map.

Hard vs. Soft self-attention. A hard self-attention mechanism can also be applied by masking the aligned features with the hard segmentation mask (obtained as softmax probability map). This option has the advantage of switching off possible misleading regions outside the lungs, favoring the flow of relevant regions only. Therefore the network can operate in two configurations: either with a hard self-attention scheme (HA), in which the soft-max segmentation mask (from 0 to 1) is used as a (product) weighting mask for the CXR image, or with a soft version (SA), where the segmentation mask is only

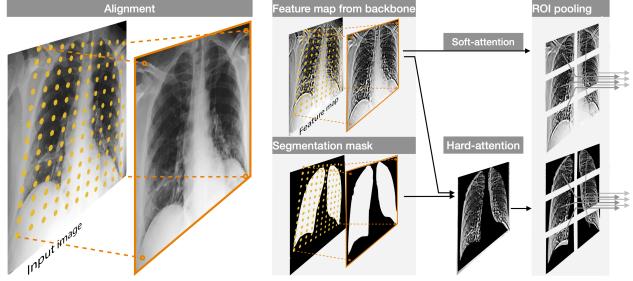


Figure 4. Example of the alignment through the sampling grid produced by the transformation matrix, and its application to both the segmentation mask and the feature maps. On the right, the hard-attention mechanism and the ROI Pooling operation.

used for spatial normalization and alignment of extracted features, but not to mask the CXR image.

ROI Pooling. The aligned (and optionally hard masked) features are finally used to estimate the 3×2 matrix containing the Brixia score. To this purpose, ROI Pooling is performed on a fixed grid with the same dimensions. In particular, lung regions are vertically overlapped by 25%, with no horizontal overlap (since the left/right boundary between lungs is easily identified, while the vertical separation presents a larger variability). This pooling module introduces a-priori information regarding the location of the six regions (i.e, A, B, \dots, F), while leaving to the network the role to correctly rearrange the lungs by means of the alignment block.

Scoring head. The final scoring module exploits the ideas of Feature Pyramid Networks (FPN) (Lin et al., 2017) for the generation of multi-scale feature maps. As depicted in Figure 3, we combine feature maps that come from various levels of the network, therefore with different semantic information at various resolutions. The presence of the alignment block, in conjunction with the optional masking, produces input feature maps that are well focused on the specific area of interest. Eventually, the output of the FPN layer flows in a series of convolutional blocks to retrieve the output map ($3 \times 2 \times 4$, i.e., 3 rows, 2 columns, and 4 possible scores $[0, \dots, 3]$). The classification is performed by a final Global Average Pooling layer and a SoftMax activation.

5.2. Loss Function and Model Training

The Loss function we use for training, is a sparse categorical cross entropy (SCCE) with a (differentiable) mean absolute error (MAE^d) contribution:

$$L = \alpha \cdot \text{SCCE} + (1 - \alpha) \cdot \text{MAE}^d \quad (1)$$

where α controls how much weight is given to SCCE and MAE^d , which are defined as follows:

$$\text{SCCE} = -\frac{1}{C} \sum_c y_c \log(\hat{y}_c) \quad (2)$$

$$\text{MAE}^d = \frac{1}{C} \left\| y - \sum_{c \in C} \frac{e^{\beta \hat{y}_c}}{\sum_{j \in C} e^{\beta \hat{y}_j}} c \right\| \quad (3)$$

where y is the reference Brixia score, \hat{y} is the predicted one, and $c \in [0, 1, \dots, 3]$ is the score class. To make the mean absolute error differentiable (MAE^d), β can be chosen to be an arbitrary large value.

The selection of such loss function is coherent with the choice to configure the Brixia score problem as a joint multi-class classification and regression. Tackling our score estimation as a classification problem allows to associate to each score a confidence value: this can be useful to either produce a weighted average, or to introduce a quality parameter that the system, or the radiologist, can take into account. Moreover, the MAE^d component, while being meaningful for the scoring system, adds robustness to outliers and noise.

Due to the nature and complexity of the proposed architecture, the training of network's weights takes place at several stages, according to a *from-the-part-to-the-whole* strategy. The different sections of the overall network are first pre-trained on specific tasks: U-Net++ is trained using the lung segmentation masks in the segmentation datasets; the alignment block is trained using the synthetic alignment dataset (in a semi-supervised setting); the classification portion (Scoring head) is trained using Brixia COVID-19 dataset, while blocking the weights of the remainder (i.e., Backbone, Segmentation, Alignment). Then a complete fine-tuning on Brixia COVID-19 dataset follows, making all weights (about 20 Million) trainable. The network hyper-parameters eventually undergo a selection that maximizes the MAE score on the validation set.

5.3. Implementation details

The network has an input size of 512×512 . The selected backbone is a ResNet-18 He et al. (2016), because it offers the best trade-off between the expressiveness of the extracted features and the memory footprint (as in the case of the input size). In the network, we use the rectified linear unit (ReLU) activation functions for the convolutional layer of the backbone, and the U-Net++, while the Swish activation function by Ramachandran et al. (2017) is used for the remaining blocks. We extensively make use of online augmentation throughout the learning phases. In particular, we apply all the geometric transformations described in Section 4.2, plus random brightness and contrast, as well. Moreover, we randomly flip images horizontally (and the score, accordingly) with a probability of 0.5. We exploit, for training purposes, two machines equipped with Titan® V GPUs. We train the model by jointly optimizing the sparse categorical cross-entropy function and MAE, with a selected $\alpha = 0.7$. Convergence is achieved after roughly 6 hours of training (80 epochs), using Adam (Kingma and Ba, 2014) with an initial learning rate of $3 \cdot 10^{-2}$, halving it on flattening. Furthermore, we set the batch size to 8.

5.4. Super-pixel explainability maps

To evaluate whether the network is predicting the severity score on the basis of correctly identified lung areas, we need a method capable of generating explainability maps with a sufficiently high resolution. Unfortunately, with the chosen network architecture, the popular Grad-CAM approach (Selvaraju et al., 2017) generates poorly localized, and spatially blurred, visual explanations of activation regions, as it happens for example also in (Oh et al., 2020). For these reasons, we designed a novel method for generating useful explainability maps. Loosely inspired by the LIME (Ribeiro et al., 2016) initial phases, we first generate a partitioning scheme of the segmented and aligned lungs using Quick-shift (Vedaldi and Soatto, 2008). For each of the N generated super-pixel, we create an image with the corresponding super-pixel set to zero value (super-pixel-masked image), and for such N images we predict the six-valued Brixia score (thus excluding the specific super-pixel from the computation). We then accumulate the differences with respect to the predicted values considering the whole original images for each score

class on the specific super-pixel. Given S the set of super-pixels, the output explanation map E is obtained as:

$$E = \sum_i^{|S|} S_i \cdot (p_i - p_0) \quad (4)$$

where p_0 is the probability map obtained with the original input, while p_i is the probability associated to the super-pixel-masked image. Intuitively, the obtained map highlights the region that most accounts for the final score. Examples can be appreciated in Figure 2 (bottom-right) as well as in Figure 9: the more intense the color, the more important the region contribution to the score decision.

6. Results

Through an articulated experimental validation we first consider how single components of the architecture operate (Sections 6.1 and 6.2) and we give a complete picture of the severity assessment performance referred to the whole collected dataset (Section 6.3). Then we deal with the inter-rater variability issue and demonstrate that the proposed solution overcomes the radiologists' performance on a consensus based Gold Standard reference (Section 6.4). We then widen the scope of our results in two directions: 1) we consider other proposed severity scores and give measures, observations, and comparisons that clearly support the need of dedicated solutions to the COVID-19 severity assessment (Section 6.5); 2) we consider the portability (both direct or mediated by a fine-tuning) of our model on public data collected in the most different locations and conditions, verifying a high degree of robustness and generalization of our solution (Section 6.6). Qualitative evidences of the role that the new explainability solution can have in a responsible and transparent use of the technology are then proposed (Section 6.7). We conclude with an ablation study essentially aiming at showing how the complexity of our multi-network architecture is neither over- nor under-sized, but it is adequate to the needs and complexity of the target visual task (Section 6.8). All results presented in this section are discussed in the following Section 7.

6.1. Lung segmentation

The performance of the segmentation stage shows totally comparable results with respect to state-of-the-art

methods (Candemir and Antani, 2019), both DL based (Zhou et al., 2018; Frid-Adar et al., 2018; Oh et al., 2020), and hybrid (Candemir et al., 2014). Table 4 reports the results for the U-Net++ (and U-Net comparison) in terms of Dice coefficient and Intersection over Union (IoU), aka Jaccard index, obtained on the test set of the segmentation datasets (Sec.4.1). Training curves for the segmentation task (on both training set, and validation set), tracking the IoU, are shown in Figure 7-a for BS-Net in HA configuration.

Table 4
Lung segmentation performance.

	Backbone	Dice coefficient	IoU
U-Net++	ResNet-18	0.971	0.945
U-Net	ResNet-18	0.969	0.941

6.2. Alignment

After training on the synthetic dataset described in Section 4.2, we report the following alignment results: Dice coefficient = 0.873, IoU = 0.778. Given the difficulty of the task and the fact that simulated transforms are usually overemphasised with respect to misalignment found in real data, this apparently fair performance is fully satisfactory in our context. Moreover, during a visual check on all 4,707 images in the Brixia Covid-19 dataset, no impairing misalignment (lung outside the normalized region) was observed. Residual errors are typically in the form of slight rotations and zooms, which are not critical and well tolerable in terms of overall self-attentive behavior. Training curves for the alignment task (on both training set, and validation set), tracking the IoU, are shown in Figure 7-b, always for HA configuration. Convergence behaviors are clearly visible, with a consolidating residual distance between training and validation curves.

6.3. Score prediction on Brixia COVID-19 dataset

To evaluate the overall performance of the network, we analyze the Brixia score predictions with respect to the score assigned by the radiologist(s) R_0 , i.e. the one(s) who originally annotated the CXR during the clinical practice. Discrepancies found on the 449 test images of Brixia COVID-19 dataset are evaluated in terms

Table 5

Brixia score prediction performance parameters for the four considered models on the Brixia COVID-19 dataset (only blind test set results reported). Parameters are evaluated on each single lung region (A-F), averaged on all the lung regions and on the Global Score (P-value $\ll 0.00001$ everywhere).

		A	B	C	D	E	F	Avg. on regions	Global score
BS-Net-Ens	MER	0.169	-0.038	-0.056	0.125	-0.045	-0.192	-0.006	-0.036
BS-Net-SA		0.107	-0.087	-0.171	0.082	-0.129	-0.343	-0.090	-0.541
BS-Net-HA		0.156	-0.147	-0.085	0.107	-0.016	-0.238	-0.037	-0.223
ResNet-18		0.356	-0.038	-0.056	0.125	-0.045	-0.192	0.100	0.601
BS-Net-Ens	MAE	0.459	0.448	0.412	0.374	0.459	0.494	0.441	1.728
BS-Net-SA		0.499	0.501	0.506	0.408	0.499	0.566	0.496	1.846
BS-Net-HA		0.481	0.477	0.481	0.370	0.488	0.532	0.471	1.826
ResNet-18		0.543	0.486	0.506	0.452	0.584	0.530	0.517	1.951
BS-Net-Ens	SD	0.604	0.524	0.540	0.541	0.574	0.609	0.565	1.429
BS-Net-SA		0.638	0.560	0.579	0.576	0.594	0.634	0.597	1.514
BS-Net-HA		0.613	0.575	0.583	0.552	0.594	0.616	0.589	1.505
ResNet-18		0.657	0.579	0.591	0.632	0.657	0.601	0.619	1.710
BS-Net-Ens	CC	0.675	0.779	0.731	0.682	0.737	0.672	0.713	0.862
BS-Net-SA		0.635	0.733	0.675	0.633	0.718	0.636	0.672	0.847
BS-Net-HA		0.665	0.742	0.679	0.662	0.722	0.645	0.686	0.845
ResNet-18		0.598	0.739	0.667	0.562	0.655	0.643	0.644	0.842

of Mean Error (MER), Mean Absolute Error (MAE) with its standard deviation (SD), and Correlation Coefficient (CC).

Four networks are considered for comparison, three of which are different configurations of BS-Net: the hard attention (HA) one, the soft attention (SA) one, and one ensemble of the two previous configurations (ENS). In particular ENS configuration exploits both HA and SA paths to make the final prediction (by averaging their output probabilities): these realizations are the best model with respect to the validation set, and the obtained model after the last training iteration. The fourth compared network is ResNet-18 (the backbone of our framework) as an all-in-one solution (with no dedicated segmentation, nor alignment stage), since it is one among the most adopted architectures in studies involving CXR analyses, also until today in the COVID-19 context.

Table 5 lists all performance values referred to each of the six regions (A to F) of the **Brixia score** (range [0-3]), to the average on single regions, and to the Global Score (range [0-18]). In a consistency assessment perspective, Figures 5 (top) and (bottom) show the confu-

sion matrices for the four networks related to the score value assignments for single lung regions, and for their sum (Global Score), respectively. From Table 5 it clearly emerges that the ensemble decision strategy (ENS) succeeds in combining the strengths of the soft and hard attention policies, with the best average MAE on the six regions of 0.441. Conversely, the straightforward end-to-end approach offered by means of an all-in-one ResNet-18 is always the worst option compared to the three BS-Net configs.

The error distribution analysis on MAE, depicted in Figure 6, shows the prevalence of lower error values on both single lung regions and Global Score estimations. The joint view gives another evidence that single-region errors unlikely sum up as constructive interference. Training curves for this prediction task (on both training set, and validation set), tracking the Mean Absolute Error (MAE) on the set of lung sectors are shown in Figure 7-c (HA configuration). Convergence behaviors are clearly visible, with a consolidating residual distance between training and validation curves.

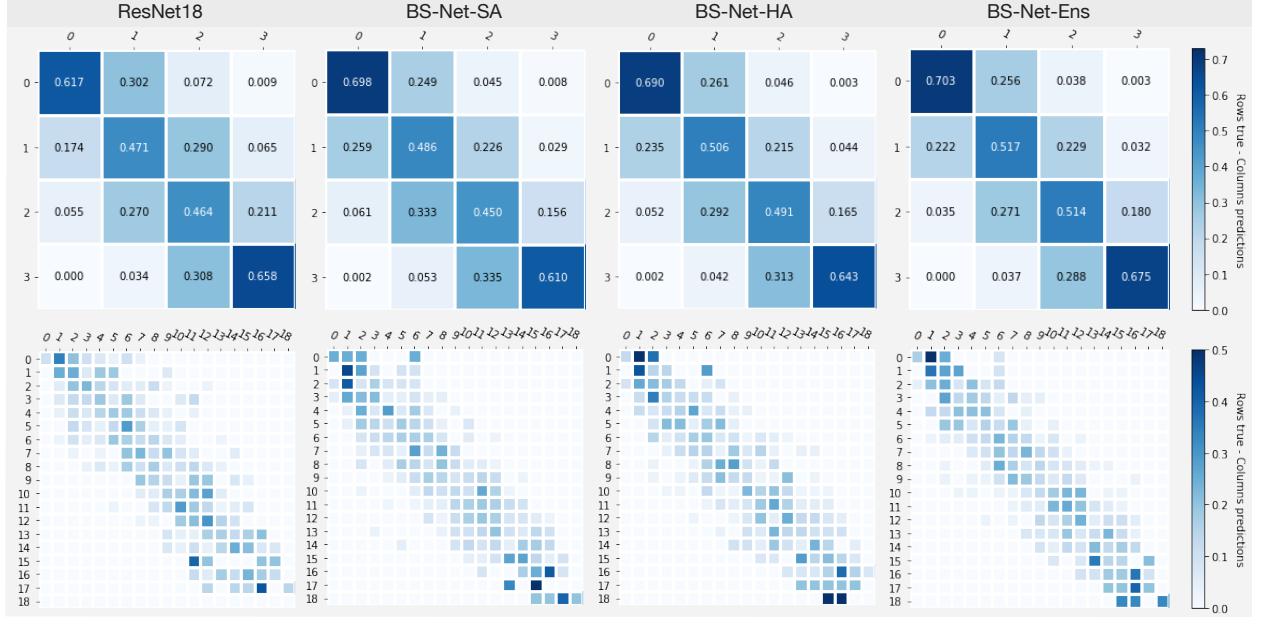


Figure 5. Consistency/confusion matrices based on lung regions score values (top, 0–3), and on Global Score values (bottom, 0–18).

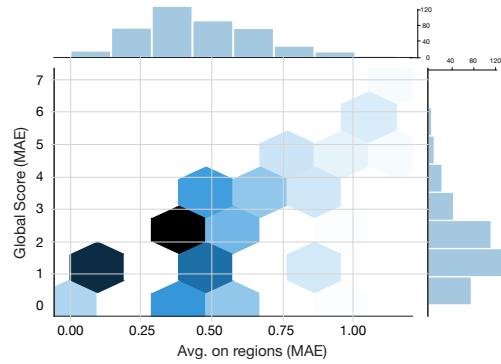


Figure 6. Single and joint MAE distribution for lung regions and Global Score predictions obtained by BS-Net (ENS).

6.4. Performance assessment on Consensus-based Gold Standard

Results in Table 5 are computed with respect to the score assigned by a single radiologist (i.e., R_0) among the ones in the whole staff. With the aim of providing a more reliable reference, we consider the Consensus-based Gold Standard (CbGS) dataset (Sec.4.3.1). This allows to recompute the BS-Net (ENS) performance on a subset of 150 images, which are annotated with multiple ratings (by R_0, R_1, R_2, R_3 , and R_4) from which a consensus reference score is derived. Table 6 (top-center) clearly shows a significant improvement on MAE with respect to the comparison versus R_0 only (0.424 vs. 0.452).

Inter-rater agreement: human vs. machine performance. In Figure 8 we assess the inter-rater agreement by listing MAE and SD values referred to all possible pairs of raters, including R_0 , and also BS-Net (ENS), as a further “virtual rater”. Looking at how BS-Net behaves (orange boxes in Figure 8), we observe the level of agreement reached between the network and any other rater is, almost always, higher than the inter-rater agreements between any pair of

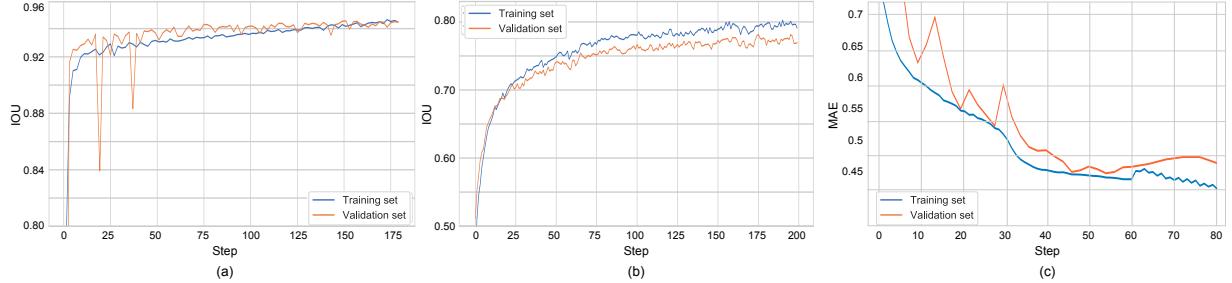


Figure 7. Training curves related to BS-Net-HA. Segmentation (a); Alignment (b); Brixia score prediction – best single model (c).

Table 6

Results on the Consensus-based Gold Standard dataset (150 images): (top) performance of BS-Net (ENS) computed on the Consensus-based Gold Standard; (center) performance of BS-Net (HS) vs original rater R_0 ; (bottom) averaged performance of all R_i vs CbGS

	MEr	MAE	SD	CC
BS-Net (ENS) vs. CbGS				
Avg. on reg.	-0.133	0.424	0.580	0.743
Global score	0.800	1.787	1.354	0.907
BS-Net (ENS) vs. R_0				
Avg. on reg.	-0.019	0.452	0.575	0.754
Global score	-0.113	1.847	1.553	0.834
Average on all pairs of radiologists				
Avg. on reg.	-0.131	0.528	0.614	0.736
Global score	-0.784	2.592	1.965	0.835

human raters. For example, by considering R_0 as a common reference, we have an equal performance only in the case of R_4 . Table 6 confirms how BS-Net (top) performs on average significantly better (MAE 0.424) with respect to the global indicators (bottom) coming from averaging all pairwise R_i vs R_j ($i \neq j$) comparisons (MAE 0.528).

The inter-rater agreement values (between human raters) indicates a fair to moderate level of agreement (both averaged two-raters Cohen's kappa value and multi-rater Fleiss' kappa value, based on single cell scores, are around 0.4). On the one hand, this is a confirmation that the Brixia score, probably succeeds in reaching the though compromise between maximizing the score expressiveness (spatial and rating granularity) while keeping under control the level of subjectivity (inter-rater vari-

	Avg. on regions				Global Score					
	R_1	R_2	R_3	R_4	BS-Net _{Ens}	R_1	R_2	R_3	R_4	BS-Net _{Ens}
R0 -	0.55 (0.63)	0.47 (0.56)	0.58 (0.65)	0.45 (0.58)	0.45 (0.58)	2.58 (1.93)	2.31 (2.19)	2.86 (2.19)	2.05 (1.61)	1.85 (1.55)
R1 -		0.37 (0.52)	0.56 (0.68)	0.60 (0.62)	0.52 (0.64)		1.53 (1.38)	2.84 (2.35)	2.93 (2.07)	2.28 (1.65)
R2 -			0.58 (0.65)	0.54 (0.59)	0.45 (0.55)			3.07 (2.40)	2.85 (1.88)	2.08 (1.58)
R3 -				0.58 (0.66)	0.56 (0.67)				2.89 (2.05)	2.60 (1.71)
R4 -					0.42 (0.55)					1.77 (1.43)

Figure 8. Pairwise inter-rater results in terms of MAE (and SD). In the most right column (orange), the inter-rater results with predictions by BS-Net-Ens.

ability). On the other hand, measured inter-rater variability levels constitute a clear limitation that bound the network learning abilities, concurrently allowing to assess whether the network surpasses single radiologists performance. The opportunity for the network to learn not only from a single radiologist but virtually from a fairly large community of specialists (being R_0 a varying radiologist) is, de facto, the margin that we have been able to exploit.

6.5. Performance assessment on other severity scores

In Table 7 we show the performance related to six-valued T score, akin to the score presented in (Toussie et al., 2020), derived by thresholding the Brixia score as described in Section 3.2. We provide results on both the whole Brixia COVID-19 test set and on the Consensus-Based Gold Standard set. Interestingly, the correlation increases from 0.73 on the whole test set to 0.81 on the

Table 7

T score performance (faithful simulation of the score proposed in (Toussie et al., 2020)).

	MEr	MAE	SD	CC
BS-Net-ENS on the whole test set				
Avg. on reg.	0,009	0,147	0,349	0,51
Global score	0,056	0,742	0,921	0,728
BS-Net-ENS on the CbGS set				
Avg. on reg.	-0,074	0,174	0,38	0,563
Global score	-0,447	0,94	1,07	0,81

CbGS set, while MAE, despite maintaining acceptable values, increases as well (probably due to a residual from a non perfect mapping between the two scores).

In Table 8 we simulate the computation of the L0 score by Brixia score mapping followed by linear regression (see Sec.3.2). Thanks to annotations we provided for CXRs in the dataset by (Cohen et al., 2020c) we had the possibility to perform a direct comparison with the non-specific method described in Cohen et al. (2020a) from which we report only the best results. We report the results produced by BS-Net-ENS on the intersection between the subset of the Cohen dataset considered in our work (Sec.4.4) and the CXRs we found used in Cohen et al. (2020a) (a retrospective cohort of 94 PA CXR images). We also produce the results considering the whole subset for which we produced Brixia score annotations (obtaining virtually equivalent results). We also report L0 score related results starting from Brixia score assigned by our experts. The performance boost produced by a prediction from a specifically designed solution is evident, and this is coherent also to the considerations and limitations acknowledged by the authors of Cohen et al. (2020a).

6.6. Public COVID-19 datasets: portability tests

The aggregate public CXR dataset (Cohen et al., 2020b), described in Section 4.4, has been judged as inherently well representative with respect to the various manifestations degrees of COVID-19. For this reason, it represents a good test bed to assess model portability. Exploiting the two independent Brixia score annotations of this dataset (one from a senior R_s , and another

from a junior radiologist R_j), we performed a portability study, with the aim of deriving some useful guidance for extended use of our model on data generated in other facilities. In particular, we carried out three tests on BS-Net (HA configuration) measuring the performance on: 1) the whole set of 192 annotated images (full); 2) a reduced test set with fine-tuning, after random 75/25 splitting (subset, fine-tuning); 2) a reduced test set with partial retraining of the network, after random 75/25 splitting, with segmentation and alignment blocks trained on their specific datasets (subset, from scratch). In reporting results, we considered the senior radiologist R_s as the reference in order to have the possibility to assess the second rater R_j performance the same way we assess the network performance. Table 9 lists all results from the above described tests.

Looking at results on the full dataset, we can derive that, even by directly applying the model trained on the Brixia COVID-19 dataset on a completely different dataset (and collected in a highly uncontrolled way), the network confirms the meaningfulness of the learning task and shows a fair robustness to work in different context even in an uncontrolled way. On the other hand, the skilled human observer confirms higher generalization capability, with a MAE of 0.405 on the full dataset. On the reduced subset, when retrained from scratch, the network is not able anymore to produce even the results obtained by the same model trained on the Brixia COVID-19 dataset: a clear evidence of the need to work with a large dataset and of the adequate capacity of our model. This is further confirmed by looking at the fine-tuning results, where the network reaches the best performance (MAE 0.465) by exploiting an already trained baseline.

6.7. Explainability maps

In Figure 9 we illustrate some explainability maps generated on Brixia COVID-19 data: three are exact predictions (top), while two are chosen among the most difficult cases (bottom). Along with maps, we also report the related lung segmentation and alignment images. Such maps, obtained as described in Section 5.4, clearly highlight the regions that triggered a specific score: they are drawn with the colour of the class score (i.e., 1 = orange, 2 = red, 3 = black) in case they significantly contributed to the decision for that score, while a white coloured region means that it gave no contribution to such score decision.

Table 8
Opacity score linear regression from global **Brixia score**.

	Correlation	R^2	MAE	MSE	coef	intercept
from						
Best (Cohen et al., 2020a)	0.80±0.05	0.60±0.17	1.14±0.11	2.06±0.34	–	–
BS-Net on Cohen set	0.84±0.05	0.54±0.17	0.67±0.10	0.68±0.18	0.31±0.01	0.15±0.08
BS-Net on our subset	0.85±0.08	0.53±0.24	0.67±0.12	0.67±0.22	0.31±0.01	0.09±0.09
R_s on our subset	0.90±0.06	0.72±0.13	0.55±0.10	0.45±0.15	0.28±0.01	0.55±0.07

Table 9

Portability tests on the public dataset (Cohen et al., 2020b). MAE and its SD are listed for both reporting radiologist R_j and BS-Net-HA. The network has been used in three training conditions: 1) as is, originally trained on the Brixia COVID-19 dataset (full), 2) fine-tuned on the public dataset (subset, fine-tuning), and 3) completely retrained, classification part only, on the public dataset (subset, from scratch).

	Test	A	B	C	D	E	F	Avg. on regions	Global score
Radiologist R_j	full	0.135	0.182	0.156	0.115	0.177	0.021	0.131	0.786
	subset	0.149	0.234	0.191	0.000	0.191	0.021	0.131	0.787
BS-Net-HA	MEr	full	0.177	-0.167	-0.177	0.167	-0.208	-0.651	-0.143
		subset	0.125	-0.104	-0.188	0.167	-0.063	-0.583	-0.108
* from scratch		subset	0.208	0.396	0.104	0.250	0.042	0.063	1.063
		subset	0.146	0.167	-0.042	0.229	0.167	-0.208	0.076
Radiologist	full	0.396	0.401	0.438	0.333	0.396	0.469	0.405	1.974
	subset	0.404	0.447	0.489	0.340	0.362	0.447	0.415	1.851
BS-Net-HA	MAE	full	0.521	0.438	0.552	0.385	0.438	0.776	0.518
		subset	0.458	0.479	0.521	0.375	0.479	0.625	0.490
* from scratch		subset	0.375	0.646	0.604	0.458	0.542	0.479	0.517
		subset	0.479	0.500	0.500	0.354	0.458	0.500	0.465
									2.000

The first row of Figure 9 offers a clear overview of the agreement level between the network and the radiologist in shift (R_0). Conversely, the two cases in the bottom row of Figure 9 evidences both under- and over-estimations in single sectors, despite producing a correct Global Score in the case on the left.

6.8. Ablation study

Adopting BS-Net in the HA configuration, we conducted an ablation study comprising two sets of experiments, which are carried out on the training (3,313 CXRs) and on the validation (945 CXRs) sets of the Brixia COVID-19 database.

Feature Extraction. This set of experiments investigates on the type and complexity of the feature map extraction

leading to the **Brixia score** estimation (see Scoring head in Section 5.1). We then compare the adopted FPN-based solution with three different configurations. The first, simplified, configuration gets rid of the multi-scale approach, so that the score estimation exploits the features extracted by the backbone head. The second, more complex, configuration envisages an articulated multi-scale approach based on the EfficientDet (Tan et al., 2019), where BiFPN (Bidirectional FPN) blocks are introduced for an easy and fast multi-scale feature fusion. The third configuration adds one resolution level to the FPN to allow the flow of $1,024 \times 1,024$ images. Results on this benchmark are reported in Table 10. While the first simplified configuration produces an improved MAE on the training set, we observe a poorer generalization capability

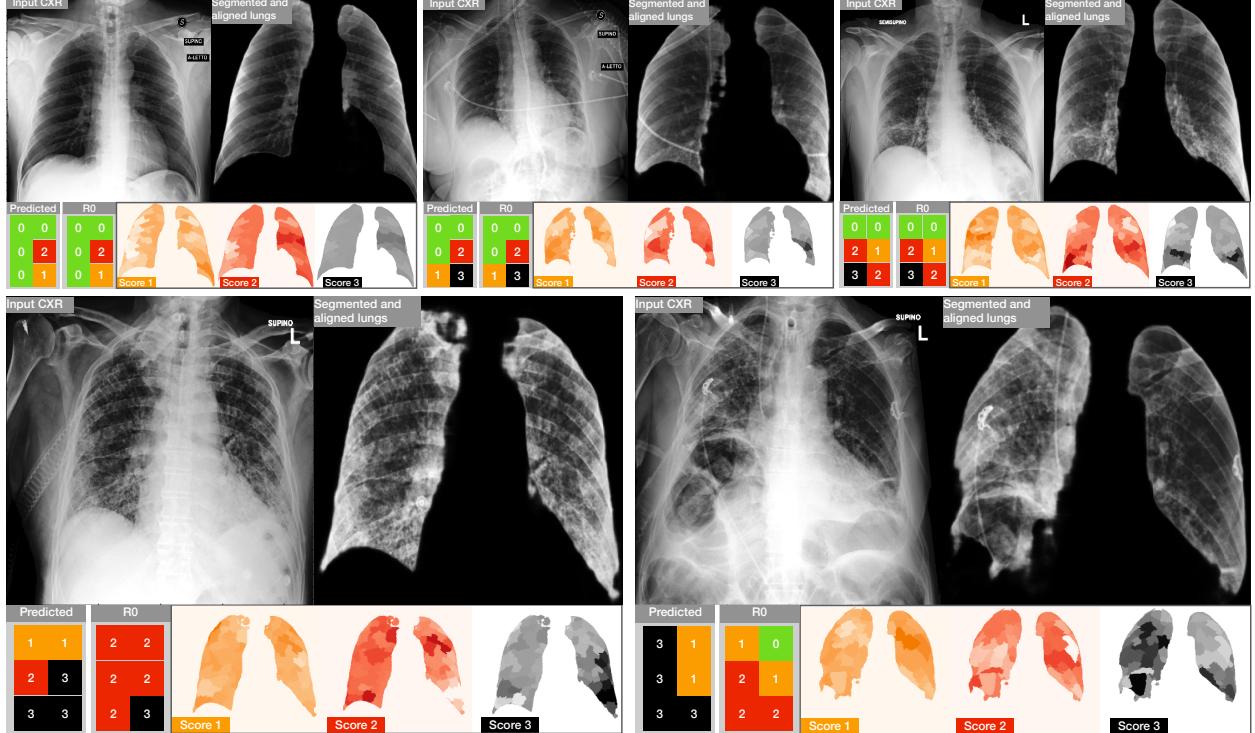


Figure 9. Results and related explainability maps obtained on five examples from the Brixia COVID-19 test set. (top) Three examples of accurate predictions. (bottom) Two critical cases in which the prediction is poor with respect to the original clinical annotation R_0 . For each block, the most left image is the input CXR, followed by the aligned and masked lungs. In the second row we show the predicted Brixia score with respect to the original clinical annotation R_0 , and the explainability map. In such maps the relevance is colored so that white means that the region does not contribute to that prediction, while the class colour (i.e., 1 = orange, 2 = red, 3 = black) means that the region had an important role in the prediction of the T score class.

on the validation set. The complex configuration, instead, produces a worsening on both data sets. Therefore FPN confirms to be a good intermediate solution between the latter two configurations. Eventually, adding one resolution level produces again a performance worsening (this is a confident indication despite, for memory limitations, we did not succeed in performing a complete fine-tuning).

Data Augmentation. The second investigated matter regards whether the pre-processing and augmentation policies we adopted are effective, or if there are some prevailing or redundant constituents. In Table 11 we present the results of performed experiments which combines different augmentation policies: it is clearly evident that partial augmentation policies are not adequate, since they pro-

Table 10
Performance on the training and validation set for different Feature Pyramid Networks (or lack of).
(*) No complete fine-tuning due to memory limitation

	Train MAE (SD)	Val MAE (SD)
FPN (adopted)	0.455 (0.578)	0.469 (0.583)
Backbone head	0.395 (0.542)	0.475 (0.592)
BiFPN	0.486 (0.593)	0.504 (0.598)
FPN 1024 (*)	0.498 (0.564)	0.498 (0.589)

duce performance worsening on the validation set, and tend to create overfitting gaps between training and validation performance. Conversely, their joint use produces best results and not such a gap. Moreover, we can appre-

ciate the impact of the pre-processing equalization, which is able to correctly handle the grayscale variability in the dataset.

Table 11
Performances on the training and validation set for different augmentation policies.

	Pre proc.	Train MAE (SD)	Val MAE (SD)
No augmentation	y	0.306 (0.490)	0.528 (0.610)
Bright. & contrast	y	0.341 (0.518)	0.550 (0.628)
Geometric transf.	y	0.272 (0.460)	0.541 (0.623)
All together	n	0.437 (0.585)	0.571 (0.645)
All together	y	0.455 (0.578)	0.469 (0.583)

7. Discussion

We have introduced an end-to-end image analysis system for the assessment of a semi-quantitative rating based on a highly difficult visual task. The estimated lung severity score is, by itself, the result of a compromise: on the one hand, the need for a clinically expressive granularity of the different stages of the disease; on the other hand, the built-in subjectivity in the interpretation of CXR images, stemming from the intrinsic limits of such imaging modality, and from the high variability of COVID-19 manifestations. As an additional complication, the available **Brixia score**, even if coming from expert personnel, has neither ground truth characteristics (as ratings are affected by inter-observer variability), nor it is highly accurate in terms of spatial indication (since scores are related to generic rectangular regions).

The best performance in the prediction of the **Brixia score** is obtained, in all tests, by using an ensemble decision strategy (ENS). Reported mean absolute errors on the six regions are: MAE=0.441, when compared against the clinical annotations by radiologist R_0 on the whole test set of 450 CXRs; and MAE=0.424 when compared against a Consensus-based Gold Standard set of 150 images annotated by 5 radiologists. Naively speaking, being the scoring scale defined on integers, any MAE measured on single regions below 0.5 could be interpreted as acceptable. This might appear as a simplified reasoning, but interviewed radiologists, with hundreds of

cases of experience of such semi-quantitative rating system, also indicated, from a clinical perspective, ± 0.5 as an acceptable error on each region of the **Brixia score**, and ± 2 as an acceptable error on the Global Score from 0 to 18. These indications are also backed up by the prognostic value and associated use of the score as a severity indicator that comes from the experimental evidence and clinical observations during the first period of its application (Borghesi et al., 2020a).

The above *a-priori* interpretation of “acceptable” error on a single region is clearly not sufficient. It is also for this reason that we built a CbGS. This is useful to have a reference measure of the inter-rater agreement between human annotators, acting as a boundary measure of human performance. This is relevant since, being a source of error in our weakly supervised approach, such inter-rater agreement also determines an implicit limit to the performance we can expect from the network. Tests on the CbGS confirm that, on average, the level of agreement reached between the network and any other human rater is slightly above the inter-rater agreements between any pair of human raters, thus statistically evidencing that performance of BS-Net overcome those of radiologists in accomplishing the task. This is a fundamental basis to think at clinically oriented studies in a perspective of a responsible deployment of the technology in (human-machine collaborative or computer-aided diagnosis) clinical settings. A MAE under 0.5 for both the network and radiologists is also an indirect evidence of the fact that the **Brixia score** rating system (on four severity values) is a good trade-off between the two opposite needs of having a fine granularity of the rating scale, and a good inter-rater agreement. Moreover, what comes out from the comparison with other scoring systems is that the **Brixia score** can be considered as a good super-set with respect to others. This is provided by either a good spatial granularity (over six regions), and a good sensibility (over four levels).

The fact that the ensemble decision strategy combines the strengths of the soft and hard attention policies deserves some further elaboration. In fact, if on one hand, removing the context is fine to avoid possible bias on the decision, on the other hand, the context info can help when the segmentation is too restrictive. For example, retrocardiac consolidations that could be visible are removed from the lung segmentation and therefore their as-

sessment is not allowed in the hard attention approach. This residual complementarity between the two options is exploited by the ensemble decision and this can explain the significant improvement. This also clearly justifies the more structured approach we designed, which demonstrates to pay-off right from the soft-attention configuration. Another aspect that emerges looking at MEr is that our architecture does not over/under-estimate, while the other compared architecture (ResNet-18) tends to overestimate. A last qualitative evidence in favor of the use of the composite loss function of Equation 1, comprising an additional component related to the MAE, is that the performance we obtain are unbiased and stable over several repetitions of the whole training process.

Portability tests performed on public datasets can be easily turned into clear guidelines for the use of the proposed model on data originated at different facilities and/or on related clinical contexts (e.g., severity assessment of other kind of pneumonia). In fact, from collected evidence, there are all the makings of a highly portable model: performance are robust to change of settings, while fine tuning is advisable for performance optimization.

For what concerns explainability maps, this information can be used to increase trust in the outcome, and point in possible confounding situations. We had a valuable positive general feedback from radiologists that considered these maps as a possible complementary source of visual attention and of second level reasoning in a possible scenario of computer-assisted diagnosis. Looking for example at Figure 9, some additional considerations are possible. The case on the bottom-left part, despite producing a correct Global Score (considered a positive fact by the radiologists, given the specific case), evidences both under- and over-estimations in single sectors. Reviewed by a senior radiologist, this case evidenced some problematic areas even for the radiologists that are often called to express an average score about what they see in different areas. For this reason the super-pixel explainability maps constitute a useful machine-human communication tool. In particular the sector A interested by the presence of an assisted ventilation device can determine a common problem for both machine an expert, but the machine proves to not diverge toward unduly high ranking, while the expert ruled in favor to the machine in the other upper lung sector (D), while confirms a slight overestimation in sec-

tor E. In general, we can appreciate the fact that external equipment do not harm the prediction, nor produces unwanted biases as in Figure 9(top-middle, bottom-left, bottom-right). The last case (bottom right) evidences a segmentation error on the right lung, since part of the colon (filled by air, pulling up the diaphragm and compressing the lung) enters in the segmentation mask, determining a wrong evaluation of the corresponding area. However, the radiologist positively considered the fact that the system sees a difference of two levels between the upper lung portions, which the expert considered a more coherent judgment at a second view. From these qualitative observations and explainability map support, we can conclude that, despite the automated AI-driven scoring is not meant to eliminate the evaluation of the radiologist, it can be used to aid and streamline the reporting workflow, and improving the timeliness of first evaluation, by proposing a preliminary interpretation of findings. Such aid might also prove useful in case of shortage of radiologists, condition that might be worsened due to the spread of contagion among physicians.

The main limitations of this work are related to residual errors. Despite highly aligned with radiologists' performance and not evidencing statistical biases, a case-by-case deeper comparison of possible causes of error could guide further improvement of the image analysis architecture. In particular, since the segmentation task is sometimes ambiguous and hard to accomplish, better solutions should be designed to handle anomalies in the segmentation results.

8. Conclusions and future directions

Our study for the estimation of a semi-quantitative rating of lung severity is justified and driven by the strong clinical reasons related to the role of CXR images for the management of COVID-19 patient monitoring, especially in conditions of overloaded healthcare facilities. Working with a very large dataset of almost 5,000 images allowed to develop a solution which deals with all aspects of the problem, also thanks to other datasets which are exploited in a hierarchical end-to-end training process. The prospected solution is designed to work in a weakly supervised context and to be capable of manifesting self-attentive abilities on data directly coming from all CXR

modalities/devices and in all clinical and patient care conditions. Having tested architectural variants, and targeted ablation studies, the network performance ultimately surpasses qualified radiologists in rating accuracy and consistency. We also collected evidences of the robustness and portability of the model, that favorably highlights its application to other clinical settings. All annotated CXRs and the proposed models are made available for research purposes⁹.

Regarding future work, observed results constitute a strong basis in a perspective of more clinically oriented validations and in a perspective of trustable and responsible deployment. An interesting clinical scenario to evaluate is the following: whether, in case the BS-Net follows the same patient, it could exhibits greater self-coherent behavior if compared to the case where serial CXR acquisitions are reported by different radiologists (according to availability and working shifts). Another direction to consider is the possibility to exploit CT images from COVID-19 patients to derive semi-quantitative ground truth information directly from the quantitative volumetric assessments.

Declaration of Competing Interest

None.

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⁹Note for reviewers: the dataset is subject of a separate data-only journal submission while models will be released upon acceptance of this paper.

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