Original Article

Diagnostic accuracy of MIP slice modalities for small pulmonary nodules in paediatric oncology patients revisited: What is additional from the paediatric radiologist approach?

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ABSTRACT

Background: Maximum intensity projection (MIP) CT image reconstruction is a beneficial diagnostic tool in paediatric radiology and can help to distinguish between small pulmonary nodules and adjacent vessels or pulmonary scars.

Objectives: The purpose of this study was to determine the optimal MIP slice thickness and reconstruction plane for pulmonary nodule detection in paediatric patients.

Materials and methods: Fifty-five paediatric patients with suspected nodules less than 5 mm who were diagnosed with extra-pulmonary malignancy and underwent multidetector computed tomography (MDCT) of the thorax were evaluated. Multiplanar CT 5 mm MIP reconstruction (axial-coronal-sagittal), 2 mm axial-coronal MIPs, and 1-mm and 5-mm axial source slices, were interpreted independently by three blinded radiologists. The axial -1 mm slices were accepted as the gold standard method as the result of retrospective consensus session in order to get comparison with similar studies. The number of nodules, size and location, distance from pleura, overall time taken and confidence were recorded separately for each observer.

Results: Receiver operating characteristic (ROC) analysis showed significant advantages of MIP images over averaged images. With high significance (p < 0.001), coronal 5 mm MIP reconstructions were found to be most advantageous over conventional reconstruction techniques. Mean reading time was fastest in axial 5 mm MIP images.

Conclusions: Compared to conventional paediatric chest CT reconstruction techniques, detection of pulmonary nodules with diameters smaller than 5 mm was found to be most sensitive in 5 mm coronal MIP images.

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1. Introduction

Growing and widespread availability of multidetector computed tomography (MDCT) in the past years has increased the detectability of small pulmonary nodules in...
paediatric patients [1,2]. The development of visualization techniques such as multiplanar reconstruction (MPR), maximum intensity projection (MIP) and computer-aided detection (CADe) helped to improve radiologists’ performance in detecting pulmonary nodules [3–6].

Detection of pulmonary nodules in paediatric patients suffering from extra-pulmonary malignancies is prognostically important and may influence therapy. Visualizing these changes occupies a significant amount of time in the daily routine of paediatric radiology departments. This is aggravated by the fact that children have a smaller chest size and a faster respiration, making nodules harder to detect and scanning more prone to motion artefacts [1,2,6,7]. In addition, applied doses are routinely lower than in adults which is another factor that complicates the detection of nodules due to increased image noise.

In daily practice, high resolution MDCT with narrow collimation guarantees high spatial resolution and reduced partial volume effects, both improving the probability of detecting small pulmonary nodules [8–10]. Drawbacks are the increased number of images that need to be examined by the radiologist, and thin sections that make it harder to differentiate between a lung nodule and a vessel. A solution for both issues can be MIP reconstructions. The MIP technique is based on the principal of keeping the object with the highest density per slice only [1,4,11]. The most urgent disadvantage of MIP images decreased impression of depth. On the other hand, they are believed to enable better detection of small pulmonary nodules and reduce the number of images needed to be evaluated. This is due a better traceability of intrapulmonary vascular structures and branchings, making adjacentely located nodules easy to percept. Existing studies showed that in comparison with thin section axial MDCT, axial MIP reconstructions enhanced the diagnostic accuracy of small pulmonary nodules [1,2].

The purpose of this study was to assess the possible benefits of MIP reconstructions in different imaging planes, compared to thin section axial images. Specificity, sensitivity, and accuracy of lung nodule detection among the different reconstruction techniques were therefore compared in a series of paediatric patients under observation for lung metastases of extra-pulmonary malignancies.

2. Materials and methods

Local hospital’s oncology database and Picture Archiving and Communications System (PACS) were queried for paediatric patients with extra-pulmonary solid organ malignancies, who underwent chest MDCT between January 2010 and December 2014. A resulting total number of seventy-seven studies could be retrieved. All studies and patient records were reviewed and reconfirmed by an independent radiologist (I.K.).

Pulmonary nodule definition was based on the research by Westra et al. [6,7]. Nodules had to feature sharp margins. Exclusion criteria were pulmonary nodules larger than 5 mm, a total lung nodule count of more than 4, an underlying primary lung diseases such as cystic fibrosis, and nodules with indefinite borders or ground-glass opacities. Due to these criteria 7 patients were excluded, leaving 70 patients for evaluation.

All imaging examinations were performed on a MDCT scanner (Brilliance 64; Philips Medical Solutions, Eindhoven, the Netherlands) using a single breath hold technique. Acquisition parameters were 120 peak kilovoltage (kVp) with enabled automatic exposure control (AEC), and a pitch of 1.0. Collimation was 0.9 mm. Raw image data were reconstructed to 1 mm and 5 mm axial slices, axial – coronal 2 and 5 mm MIP slices, sagittal 5 mm MIP slices.

Independently from each other, 3 blinded radiologists (M.B.O = observer 1, U.Y = observer 2, and C.K = observer 3) with varying radiological experience evaluated the data in Osirix software. Lung window settings (centre 600 HU, width 1600 HU) were applied for image interpretation. Moreover, observers were allowed freely manipulate the window settings when desired. Each dataset was checked for number of nodules, size, location (central vs. peripheral, left or right, upper, middle or lower lobe) by each of three observers independently. Required reading time was recorded too. Mean time and standard deviations for all observers were calculated. Reconstructions were analysed in a random order. Observers were not allowed to read more than 5 reconstructions per day. This was to avoid recognition of same-patient-datasets among one another. Level of diagnostic certainty and observer agreement was rated on a five point scale (1 = no nodule, 2 = no confident nodule, 3 = probable nodule, 4 = more definite nodule, 5 = definite nodule).

2.1. Statistical analysis

Statistical analysis was performed in SPSS for Windows (Version 21.0; SPSS Inc., Chicago, IL, USA).

Receiver operating characteristic (ROC) analyses were performed to assess the correct differentiation of pulmonary nodules and other structures such as lung vessels or scars. This was done in all reconstruction techniques for every observer. Area under the curve (AUC) was used to compare the performance of nodule detection and accurate differentiation of pulmonary nodules from other focal pulmonary lesions among the different reconstruction techniques. The confidence interval was defined at 99.5%. The respective analyses were performed for all observers together and were compared among each other.

Scheffé’s method was used to evaluate nodule detection confidence as a function of its orthogonal distance from the pleura. Pearson’s correlations and Friedman tests were used to assess differences between the reconstruction techniques regarding nodule detection. P values lower than 0.05 were accepted as statistically significant.

The approval for the ethics board was obtained in accordance with the local hospital guideline.

3. Results

In fifteen patients, no nodules were found correspondingly by all observers in all image review modalities (axial 1–5 mm slices, axial and coronal 2–5 mm MIP slices, and sagittal MIP image reconstructions). In the remaining 55
patients, the observers identified a total of 172 pulmonary nodules. Of the 172 nodules detected by the three reviewers at initial image interpretation, 124 were classified as “true” pulmonary nodules and the remaining 48 of the lesions were classified as pulmonary scars or vessels at the retrospective consensus reading (false positives).

3.1. Interobserver agreement

Interobserver agreement for the detection and characterization of nodules is described in Table 1. All of the correlation values were significant at the level of 0.01 which was extremely good.

3.2. Retrospective verification of nodules

ROC curves of pulmonary nodule detection in all image reconstruction techniques for all three observers are displayed in Fig. 1 (a–g) and Table 2. All review modalities except sagittal image reconstruction allowed a statistically significant differentiation between pulmonary nodules and vessels (p < 0.05).

When stratifying the data for nodule detection rate according to the localization the axial 1-mm, axial-5 mm, sagittal -5 mm MIP, axial and coronal 2 mm MIP did not show statistically significant differences. For all of these imaging modalities the area under curve was calculated as 0.5 which is less than reference line. The coronal - 5 mm – MIP images, axial - 5 mm MIP images had higher area under curve results than the reference line only for the peripheral lower parts of the specific localization. AUCs for coronal -5 mm MIP images for peripheral lower parts were 0.572 (range, 0.457–0.721) and 0.546 (range, 0.498–0.624) for axial -5 mm MIP images. These values reached statically significant p values in the differentiation of pulmonary nodules (p: 0.034 and p: 0.019, respectively).

Shortest reporting duration was observed for axial 5 mm MIP reconstructions (mean 66 ± 13 s) and longest for the sagittal 5 mm MIP images (mean 75 ± 14 s). The mean duration for the axial MIP, both 2 mm and 5 mm, was lower than the corresponding conventional axial slice techniques (p = 0.030, p = 0.042 respectively).

Mean AUC values were 0.692 (range 0.361–0.858) for observer 1, 0.665 (range 0.299–0.952) for observer 2, and 0.662 (range 0.479–0.811) for observer 3. Lowest AUC values were found in sagittal MIP reconstructions in all three observers. The highest AUC values for the observer one and three were coronal 5 mm MIP images, and axial-5 mm MIP images for observer two.

Figs. 2 and 3 display two examples of the incremental benefit of MIP review for the detection of small pulmonary nodules.

4. Discussion

Up to now several manuscripts have addressed the sensitivity of pulmonary nodule detection. The widespread methods included computer aided diagnosis, volume rendering, iterative reconstruction and even digital tomosynthesis [1,3,14,15]. The usefulness of double reading and its effects on sensitivity improvement were also described in the literature [1,16–18]. In contrast there is sparse knowledge of this topic in the paediatric age group.

Our aim in this study was to enlighten the benefits of axial and coronal MIPs in the detection of small pulmonary nodules in paediatric population over the conventional axial very thin slice thickness review to generate a sample guidance for further avoidance of unnecessary radiation exposure.

Analysis of the nodules detection reviews from the literature demonstrated that the most biggest difference was obtained in the small sized group whereas the nodules frequencies detected in the medium sized and the larger group were nearly similar. In these reviews the medium sized nodules are accepted as the diameter between the 5 and 10, and the bigger were accepted as more than 10 mm [1,2]. Therefore, the research subject did focus on the only small pulmonary nodule detection. Additionally the research population was chosen from the extrapulmonary malignancy paediatric oncology patients.

In our study, we excluded the nodules which is larger than five millimeters in diameter. In the similar studies, the nodules diameter between the 5 and 10 mm was grouped as middle size, and larger than 10 mm were named as big sized nodules [1,2]. In these two groups, nearly all the imaging modalities including MIP techniques and slice thickness reviewed and get very higher success rates. Including all of these nodule size diameters into our study group, it would not give additional information to the literature. Additionally, the most challenging part of paediatric chest imaging regarding the oncologic patients is the small sized nodules (nodule diameter smaller than 5 mm) [1,6,11,17,19]. In our study we reviewed all the imaging modalities and slice thickness including sagittal images in order to obtain the highest success clinical results avoiding the unnecessary time wasting modalities as an approach from the paediatric radiologist view.

Regarding the nodule size it has a significant implication and attention in the paediatric age group. In adults the malignant transformation is directly proportional to nodule size. Fleischner Society recommended the follow-up procedure without any risk factor up to 10 mm nodules whereas a small sized nodule such as less than 1 mm could represent dissemination of oncologic pattern [20,21]. This item either would play a role in the differentiation of an oncologic staging or a diagnosis of the malignancy. Recently improvement in the diagnosis and the changes in the clinical management of paediatric oncologic radiology practice the CT-only pulmonary nodule (not detectable.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>The r values of interobserver agreement for observational MIP study.</th>
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<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Axial -1 mm</td>
<td>0.592</td>
</tr>
<tr>
<td>Axial -5 mm</td>
<td>0.642</td>
</tr>
<tr>
<td>Coronal-2 mm MIP</td>
<td>0.612</td>
</tr>
<tr>
<td>Coronal -5 mm MIP</td>
<td>0.531</td>
</tr>
<tr>
<td>Axial - 2 mm MIP</td>
<td>0.774</td>
</tr>
<tr>
<td>Axial - 5 mm MIP</td>
<td>0.735</td>
</tr>
<tr>
<td>Sagittal - 5 mm MIP</td>
<td>0.305</td>
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in chest X-rays) evaluation. This process causes a mismatch in especially incidentally found nodules without an underlying risk-factor population where treatment issue is still in bias [6,8]. Additionally there is not still an agreement in the concerning of the treatment such as small nodules detected in paediatric oncology patients proved long-term results in large cohort population.

Regarding the issue of pulmonary nodule detection in the paediatric population, there were two most accurate studies [1,2]. Their main aim was based on hypothesis of 'the benefits of MIP reconstruction imaging is more accurate than conventional slice thickness imaging modalities'. They had done all the statics for the purpose of proving benefits of axial MIP imaging technique over the conventional imaging modality. The main aim of the study was to clarify all the points of MIP imaging reconstruction technique, therefore to avoid further unnecessary re-examination of the nodule determination. For the correspondence to other studies, axial MIP 2 mm and 5 mm images had higher AUC values compared to axial 1-mm and 5 mm. The r values of Axial MIP images for the axial-MIP images Kilburn were found nearly 0.49, but we found higher r values for the axial – MIP images. Additionally 0.49 was accepted as to be statically not significant which is under the reference AUC line of 0.5. Hereby, we discussed the detailed analysis of coronal 2 mm and 5 mm MIP imaging technique additionally.

Coronal-5 mm had the best diagnostic criteria to distinguish the pulmonary nodules from the scars and the vessels at the level of \( p < 0.001 \). This \( p \) level is the most accurate \( p \) level in the similar studies whereas the \( p \) value is used 0.05 for the cut-off value.

Fig. 1. The ROC Curve statical analysis results obtained to determine the performance of each slice thickness and modality section. Figure (a) shows the ROC Curve results for axial -1 mm thickness per each reader. Figure (b) shows the ROC Curve results for axial -5 mm thickness per each reader. Figure (c) shows the ROC Curve results for sagittal-5 mm thickness per each reader. Figure (d) shows the ROC Curve results for axial -2 mm MIP thickness per each reader. Figure (e) shows the ROC Curve results for coronal-5 mm- MIP thickness per each reader. Figure (f) shows the ROC Curve results for axial -5 mm-MIP thickness per each reader. Figure (g) shows the ROC Curve results for coronal-2 mm – MIP thickness per each reader.
To the best of our knowledge, there is not a published
article with the comparison of Multi-planar 5 mm – MIP
reconstruction (axial-coronal-sagittal), 2 mm axial-
coronal MIPs, and 1-mm and 5-mm axial source slices
were interpreted independently by three blinded radiolo-
gists. This study gives rise to the nodule detection rates
of different slice thicknesses of MIP images among them-
selves. Valencia et al. compared the axial and coronal
MIP 10 mm slices with axial 1-mm in adults [2]. Kilburn-
Toppin et al. used 2 mm axial and 10-mm MIP images in
their study based on the paediatric age group [1]. In the
comparison, axial and coronal MIP images provided higher
nodule detection rate and accurate differentiation of pul-
monary nodules from other focal lesions such as vessels
and scars. The reconstructed MIP images provide a higher
differentiation between the pulmonary parenchyma and
the vascular structures by selecting the highest intensity
in the voxel which enables a clear background whereas
the observers had to look at a complex one [1,10,12]. Prob-
ably this fact is the underlying basic mechanism of the
highest success of MIP slices independently in relationship
within the slice thickness and anatomical plane. Addition-
ally this could explain the higher ratio of observer agree-
ment in the MIP slices.

Table 2
The ROC curves of pulmonary nodules for image reconstruction techniques
for all three observers.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
</tr>
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<tbody>
<tr>
<td>Coronal - 5 mm MIP</td>
<td>0.775</td>
<td>0.771</td>
<td>0.811</td>
</tr>
<tr>
<td>Axial - 1 mm</td>
<td>0.665</td>
<td>0.517</td>
<td>0.767</td>
</tr>
<tr>
<td>Axial - 5 mm</td>
<td>0.572</td>
<td>0.522</td>
<td>0.623</td>
</tr>
<tr>
<td>Coronal - 2 mm MIP</td>
<td>0.707</td>
<td>0.566</td>
<td>0.886</td>
</tr>
<tr>
<td>Axial - 2 mm MIP</td>
<td>0.764</td>
<td>0.668</td>
<td>0.936</td>
</tr>
<tr>
<td>Axial - 5 mm MIP</td>
<td>0.716</td>
<td>0.552</td>
<td>0.854</td>
</tr>
<tr>
<td>Sagittal - 5 mm MIP</td>
<td>0.378</td>
<td>0.311</td>
<td>0.460</td>
</tr>
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Fig. 1 (continued)
increase the number of slices to search for [1,2,12,15]. The MIP slices are created over the final axial thin-slab images. Number of MIP images reaches marked very low numbers and rates compared within the conventional sequences. Therefore the time requirement to image interpretation for axial -MIP slices was statically significant lower than that from the axial 1 mm and 5 mm slices. The minimum duration for the axial -5 MIP images was lower than the other MIP imaging techniques; however, the sagittal images took the most longer time to evaluate. Additionally the r correlation factors were the lowest for the sagittal imaging. Both of these findings support the hardness of image interpretation from the sagittal images.

Regarding the confidence levels there were not higher improvement levels as the expected levels in the usage of axial -2 mm MIP images which could be due to previously selection of nodules on axial images which are also the main source for the MIP datasets. The MIP images were obtained from the axial source datasets. These axial thin slices have a high confidence level for the bigger size nodule detection.

Previously Valencia et al., Kilburn-Toppin et al. used 10 mm – MIP image reconstruction technique [1,2]. They found statically significant p values for the nodule detection but in our study the axial -2 mm MIP images and axial -5 mm MIP s did not evaluate to get significant p values. On the other hand coronal -5 mm – MIP results were the only significant p values at the 0.001. These results suggest that in nodule detection the smallest MIP slice technique does not validate the best optimising or highly expected values. This could be due to partial volume effect of the MDCT. In the basic the chosen slice thickness could not be higher enough to get the statically significant values. Valencia et al. used 4 row-slice MDCT, on the other hand Kilburn-Toppin used 64 row- MDCT which is the similar row-CT within us. The higher rows MDCT would give better nodule detection rates within the lower slice thickness rates. This issue should be obtained in the large cohort studies. Kilburn-Toppin et al. and Valencia et al. mentioned that the MIP images were used for as the complementary sets over the source thin slice images[1,2]. They suggested to confirm the presence of pulmonary nodules should be checked on both axial and MIP images together. To our study, we should have to point out a new comment for this sentence as the ‘addition of coronal -5 mm MIPs datasets for the small nodule detection’.

In paediatric population one of the major problem is to acquire the ideal CT scanogram without any artefact. Because of inability to hold breath there are several respiratory artefacts [1,2,11,12]. However this artefact causes a higher ratios of undiagnostic sequences therefore most of them are not included in the study. In our statical analyses we found no correlation with nodule detection rate and the cardiac artefact fact on both the MIPs and axial image interpretation. This finding is similar to Kilburn-Toppin’s study [1]. However we mention that the study material in both two studies are 64- slice multidetector row-CT which is capable of cardiac CT examination only in seconds.

Regarding the nodule detection aiming the localization only the coronal-5 mm MIP and axial-5 mm MIP imaging reached statically significant values. Additionally they
were able to obtain significant values only in the peripheral parts of the lung segments. The central part of the lung is crowded due to small chest size. Thereby it could be quite difficult to distinguish the nodule discrimination in this part [1]. Like similar studies our success rate obtaining the central part of the lung is also very low [1,2]. In the peripheral part of the lung the diameter of the vessels are in the sub-millimetric values. The volumetric value of the lung is increasing in the lower parts of the lung compared with the apical segments due to the anatomical evaluation. Thereby, it is under stable to get significant values in the lower peripheral parts of the lung. Therefore the slice thickness less than 5 mm with and without MIP reconstruction did not able to reach a significant p value.

On the other hand, it is easier to detect peripheral nodules from the other focal pulmonary nodules such as vessels or scars whereas the pulmonary nodules diameters decrease in the peripheral parts of the lungs. Regarding the pulmonary chest volume its narrower size compared with the adult size, and it is logical that crowding of the pulmonary vessels and increment of the diameter especially at the central part could be an acceptable reason for the success of decrease of the MIP images as not higher expected. In the literature there is not a quantitative analysis of this item and its effect on nodule reading performance. Kilburn-Toppin also discussed this subject in their paper and mentioned for large cohort studies [1].

The extra-pulmonary malignancy chest nodules in paediatric age group tend to locate peripherally, small and non-calcified ones [1,4–6,22].

In our series the number of pulmonary nodules with calcification was seven. The number of nodules did not allocate to reveal a statically significant p value to observe a diagnostic compromising knowledge. The original articles pointing out the findings of incidental pulmonary nodules in the paediatric population showed that in non-malignancy population, the minimum age of presentation for calcification was six years [6,23]. In our population the minimum age for the calcification was seven years which supports their findings. The major differentiation from the other studies was the study population regarding the nodules caused as a result of malignancy. The pulmonary nodules in the osteosarcoma population show calcification in the late adolescent age group is usually accepted as benign [17,24]. On the other side there is not a certain diagnostic issue to figure out the pulmonary nodules based on malignancy or benign conditions regarding the uncalcified nodules in the paediatric population.

MIP Images, acquired from 10 mm section thickness, are known to reduce interobserver inconsistency in adult populations when used along with the axial images. In addition to section thickness, section plane is also important. Axial MIP images are more preferred than coronal MIP images, while in adolescents MIP images with a

![Fig. 3.](image-url)
15 mm section thickness have similar features to axial images of 5 mm concerning detection of diagnostic nodule; evaluation of MIP images in a relatively short time is seen as a positive point. But when the infant pectoral volume and dimension in infancy are taken into consideration, a section thickness of 15 mm is accepted as being rather thick [1,2,6,11–13]. In paediatric radiology practice, there are different views regarding MIP images’ section thickness and section plan in detection of thoracic nodules. The major limitation of the research papers aiming to ‘nodule detection and measure the performance of radiologists’ is that there is not a real gold standard measurement criteria, in other words the absence of the histopathological confirmation. All of these studies accept the consensus of the observers in axial 1 mm thin slices. Therefore there is lack of false negative results which is a major determination factor of statistical analyses. One of the limitations of our study was to point out the most appropriate diagnostic tool to make difference between the benign or malign nodules in the paediatric malignancy population. The better design of this study could be based on only ‘proved malignancy nodules less than 5 mm’ which would be more accurate. Because in paediatric oncology practice one of the most challenging issues is treatment algorithm for the non-proved small pulmonary nodules. These issues could lead to overrated diagnosis for the paediatric patients which results unnecessary explosion of the chemoradiotherapicagents. PET/CT with higher than 3 SUVs is usually accepted as malignancy criteria [24]. But this is not a certain accepted issue in the paediatric oncology practice.

One of the limitation of the study is about the duration of the time mentioned in the context of minutes. These minutes would probably not reflect the exact minutes. Basically, these datasets were chosen from a selected part of specific patient group, and the timing was tested after the decision of available for review. In routine clinical practice the axial datasets are mostly ready to scan in the workstation, whereas MIP reformatting takes time depending on processor speeds. On the behalf all we mentioned in the text that the MIP images should be used to confirm the diagnosis of the axial thin slices as the complementary one. The observer management in each of the datasets was examined separately to understand whether there is a relationship between the MIP images and the gained experience.

Kilburn-Toppin et al. and Valencia et al. mentioned that the MIP images were used as the complementary sets over the source thin slice images. They suggested confirming the presence of pulmonary nodules should be checked on both axial and MIP images together.

5. Conclusion

Highest sensitivity in correct small pulmonary nodule detection was found in 5 mm coronal MIP reconstructions, which were beneficial over conventional imaging techniques. In paediatric oncology patients, we therefore recommend to add coronal 5 mm MIP reconstructions to every chest CT performed.

Conflict of interest

The author declares that there is no conflict of interest.

References


