Can iterative reconstructions improve the detection of small hypervascular liver nodules with dual-energy CT?

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Hepatocellular carcinoma (HCC) is the most common liver primary malignancy and the major cause of mortality: it’s the fifth most common cancer in men and the third cause of cancer death [1]. In many cases, hepatocellular carcinoma develops with an established background of chronic liver disease (70-90% of all patients) [2].

The use of a triphasic computed tomography (CT) scan or dynamic magnetic resonance imaging (MRI) is mandatory to make an early diagnosis of HCC. CT is more frequently used than MRI to evaluate nodules in cirrhotic patients, as it is more widely available than MRI and provides higher spatial resolution [3].

The clinical role of dynamic CT has been extensively reviewed and well established[4]. In the updated AASLD guidelines [5] only one dynamic imaging modality is necessary to make a diagnosis of HCC for nodules between 1-2 cm in diameter. If the first dynamic study shows an atypical imaging feature, the other contrast-enhanced study can be used.

For HCC detection, lesion-to-liver contrast (LCC) and lesion conspicuity on CT images is of primary importance. The arterial phase imaging is extremely important for detecting and characterizing focal liver lesions in patients with liver cirrhosis as it provides maximum contrast between an HCC and the liver parenchyma [3].

Many investigators have shown that a low tube voltage (80 kVp) CT scan can provide a better lesion-to-liver contrast (LLC) for hypervascular focal liver lesions when compared with a 120 or 140 kVp CT scan in (small to normotype) patients [6, 7]. These higher contrast values can be explained because the K edge of the iodine is closer to 80 kVp than it is to 140 kVp, therefore the attenuation of iodine-containing substances is substantially higher at 80 kVp [8].

However, the low tube voltage technique has the disadvantage of a reduced signal to noise ratio (SNR) caused by the reduced photon flux to the detectors. Thus, to realize an overall contrast-to-noise ratio (CNR) improvement for hypervascular liver lesions at lower tube voltages, the image SNR has to be increased or noise decreased, for instance increasing the tube load.

A good compromise could come from the recently developed dual-energy CT (DECT) protocols, in which two simultaneous acquisition at low and high energy (80-140 kVp) are performed [8]. Three series of reconstructed images are available with this technique: one for each acquisition dataset and a weighted averaged image from the two [9].

Another recent opportunity to improve image quality, particularly image noise and artifact, without increasing patient dose comes from iterative reconstructions [10, 11]. The Sinogram Affirmed Iterative Reconstruction (SAFIRE) developed by Siemens demonstrated the ability to improve low-contrast object detection [12], but - up to now
- no published data on kernel and strength optimization strategies (1-5) are reported in order to improve the sensitivity in the detection of liver lesions.

Iterative reconstructions may suffer from the disadvantage of an unfamiliar image appearance and switching from standard Filtered Back-Projection (FBP) to iterative reconstruction kernels could be a complex task if a standard metric is used to assess image quality. Objective physical measurements, such as image standard deviation (SD) or CNR, are difficult to relate to the overall perceived image quality or diagnostic accuracy. On the other hand, the clinical image quality evaluated with subjective scoring may be affected by many bias due to observer habits and preferences.

The purpose of this work is to optimize a DECT protocol in which iterative reconstructions are used for the detection of subcentimeter and low contrast liver lesions. Two different approaches are compared: an objective metric resulting from a human observer detectability experiment carried out simulating subcentimeter low-contrast lesions in a clinical liver image dataset and a subjective metric of image quality rating through a 5-point scale performed by the same human observers.

**Methods and Materials**

**Patient**

A woman with a confirmed diagnosis of cirrhosis who underwent triphasic liver CT scans using DECT, was selected for this study. The absence of focal lesions was confirmed by an expert radiologist. The patient was 1,62 m height and weighted 55 kg, with a BMI of 20.9 km/m$^2$.

**Scan Protocol**

Multiphasic liver CT scan was performed on a dual energy CT scanner (SOMATOM Definition Flash, Siemens) including precontrast, arterial, portal venous, and equilibrium phases. The patient was positioned supine, and an abdominal localizer scan (120 kVp and 10 mAs) was performed in order to ensure complete coverage of the liver by the field of view of the smaller detector B.

Volumes were scanned in spiral mode with a single source (120 kVp- tube A) during the precontrast, portal venous and equilibrium phase, while in the arterial phase a dual energy 80-140 kVp acquisition was performed. A summary of the acquisition protocol parameters is reported in table 1. The automatic dose modulation protocol provided by the manufacturer (CareDose 4D, Siemens Medical Solutions) was turned on.

Iodinated contrast media of 350 mgI/mL (Iomeron 350, Bracco U.K. Ltd) at a dose of 120 mL was injected using a power injector (Stellant Dual; Medrad, Indianola, PA, USA),
followed by injection of 30 to 40 mL of normal saline. The time to the arterial phase scan was determined using the bolus tracking technique (Siemens), and the scanning was automatically started 15 seconds after the attenuation coefficient of the abdominal aortic blood reached 80 HU.

The portal venous phase and equilibrium phase images were acquired 90 seconds and 180 seconds after the start of contrast injection, respectively.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Source</th>
<th>kV</th>
<th>mAs ref</th>
<th>Pitch</th>
<th>Collimation</th>
</tr>
</thead>
<tbody>
<tr>
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<td>32*1.2</td>
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<td>Portal venous</td>
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<td>80</td>
<td>360</td>
<td>0.9</td>
<td>32*0.6</td>
</tr>
<tr>
<td>Equilibrium</td>
<td>Tube B</td>
<td>140</td>
<td>139</td>
<td></td>
<td>32*0.6</td>
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</tbody>
</table>

Table 1: Acquisition protocol parameters. Precontrast, portal venous and equilibrium phases were performed in a single source mode, while the arterial phase was performed in a dual energy mode (80 kV tube A and 140 kV tube B).

Fig. 1: Acquisition scan parameters

References: Department of Radiology, University of Brescia - Brescia/IT

CT Image Reconstruction

Scan raw data were reconstructed on the workstation with the standard FBP algorithm (kernel B20) and with the recent SAFIRE algorithms. The SAFIRE algorithm represents a hybrid iterative reconstruction approach that combines a raw data iterative reconstruction with an image-based iterative reconstruction loop. The term iteration refers to series of multiple passes or repetition of mathematical calculations in image reconstruction chain to achieve desired CT image quality.

The parameterization of the loops controls the strength (S) of noise reduction, which users can set on an ordinal integral scale of 1 to 5 (S1-S5), with 1 being the weakest and 5 being the strongest noise reduction [13].
The raw data of the selected patient were reconstructed with the kernels showed in table 2, for a total of 19 image series of contiguous 2-mm slice thickness. The data were reconstructed using SAFIRE reconstructions for three different noise reduction levels (S3, S4, S5) each for the kernels I30, I31 and I26. Even if some authors [13] reported that the strength 5 was associated with an excessive pixellated and blocky appearance of images, we selected it because the highest CNRs were expected, as it leads to the highest reduction in noise.

For each of the 19 series iterative reconstructions, the DE (dual-energy) images of the arterial phase were generated by linearly blending the 80 kVp (Tube A) and the 140 kVp (Tube B) raw image with a 0.5 weighting factor (DE_0.5), and only the 80 kVp raw data was reconstructed into axial 2-mm image sets.

Quantitative measurements were performed with ImageJ, a free Java software [14]: the mean CT numbers (signal) of the liver parenchyma were obtained by manually placing a total of 6 ROIs, 3 on the 2\textsuperscript{nd} segment and 3 on the 7\textsuperscript{th} segment of the liver, and averaging and recording the CT values. Areas of focal changes in parenchymal density,
large vessels, and prominent artifacts, if any, were carefully avoided. Image noise was calculated on any ROI as the standard deviation of the pixel values. The size, the shape, and position of the ROIs were kept constant among the 19 series.

**Lesion simulation and detection test**

The HCC lesions in the arterial phase were simulated as a 3 dimensions hyper-attenuating virtual spheres. 4 axial images of 2 mm thickness continuous cuts of a 6mm diameter virtual sphere were simulated. Partial volume effects due to sphere pixellization were reproduced by simulating the continuous sphere in a very fine matrix (4096x4096 pixels) and then averaging it to a coarser matrix (512x512 pixel). The axial images were then convolved with the Modulation Transfer Function of each filter in order to reproduce spatial resolution properties of the reconstruction kernels.

![Virtual sphere](image)

**Figure 3:**
A virtual sphere of 6 mm diameter was created and 4 axial images of 2 mm thickness were used to simulate a focal hyper-enhanced liver lesion.

**References:** Department of Radiology, University of Brescia - Brescia/IT

The small 6 mm diameter was chosen because this was the measure of the smallest lesion found in a previous patient study, even if, according to the updated AASLD...
guidelines [5], only one dynamic imaging test is necessary to make a diagnosis of HCC for nodules between 1-2 cm in diameter, but it is not diagnostic for smaller lesions.

A lesion to liver contrast (LLC) of +20 HU was assigned to the simulated lesions in the blended 0.5 dual-energy (DE_0.5) series and a LCC of +30 HU was assigned at the lesions simulated in the 80 kVp series. These LLC values were chosen because they were close to the limit of the human perception for standard B20f reconstructions, as found in a previous work [15].

For each kernel, a template with 8 simulated lesions was created and summed pixel-to-pixel to the image series. The positions of the simulated lesion were accurately set, avoiding areas of focal changes in parenchymal density, large vessels, and prominent artifacts.

A bespoke program written in the ImageJ environment was created and 4 abdominal radiologists (with 10 years’ experience or more) performed the detectability test. Firstly, the original images of the patient (reconstructed with the B20f and without virtual lesions) were shown to the readers. Then the 19 series with the simulated lesion were shown and radiologists were asked to detect focal lesions in a cirrhotic patient, unaware of their contrast values and their number in each series as well as the scanning and reconstruction parameters. All images were shown on diagnostic calibrated monitor (Barco, model MDCC2121) with a 1600*1200 pixel resolution at a constant lighting room condition.

When a detail in the images was perceived as a lesion, the reader selected it with the mouse so the coordinates were registered in a text-file and compared with the coordinates of the true simulated lesions. The readers were trained on 3 liver examinations, which were processed in the same manner but were not included in the statistical analysis.

**Quality Test**

The 19 image series described in the "CT Image Reconstruction" of two cirrhotic patients with a BMI < 30 kg/m² were reconstructed both with a 80 kVp and DE_0.5 protocols, for a total of 38 series. A randomly image series presentation task was set up with ImageJ, called "Quality test". At each unidentified series presentation the same 4 radiologists were asked to evaluate the noise, the spatial resolution and the overall quality of each reconstructions on a 5-point scale (figure 4).
**Figure 4:**
4 radiologists performed the quality test in which noise, sharpness and overall image quality were judged with three 5-point scales.

**Fig. 4:** Quality test

**References:** Department of Radiology, University of Brescia - Brescia/IT

**Images for this section:**

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**Table 1:**
Acquisition protocol parameters.
Precontrast, portal venous and equilibrium phases were performed in a single source mode, while the arterial phase was performed in a dual energy mode (80 kV tube A and 140 kV tube B).

**Fig. 1:** Acquisition scan parameters
<table>
<thead>
<tr>
<th>FBP</th>
<th>TUBE A (80 kV)</th>
<th>TUBE A + B DE blended</th>
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<td>S3</td>
<td>I26 S3 80 kV</td>
<td>I26 S3 DE 0.5</td>
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<tr>
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<td>I30 S3 DE 0.5</td>
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<td></td>
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<td>I31 S3 DE 0.5</td>
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<td>S4</td>
<td>I26 S4 80 kV</td>
<td>I26 S4 DE 0.5</td>
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<td>I31 S4 80 kV</td>
<td>I31 S4 DE 0.5</td>
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<td>S5</td>
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<td>I31 S5 80 kV</td>
<td>I31 S5 DE 0.5</td>
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<td>B20 DE 0.5</td>
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</table>

Table 2: The raw data of a patient were reconstructed with 19 different combination of kernel and energy source, shown in the table.

**Fig. 2:** Reconstruction kernels
Figure 3: A virtual sphere of 6 mm diameter was created and 4 axial images of 2 mm thickness were used to simulate a focal hyper-enhanced liver lesion.

Fig. 3: Virtual sphere
Figure 4:
4 radiologists performed the quality test in which noise, sharpness and overall image quality were judged with three 5-point scales.

Fig. 4: Quality test
Results

The mean noise values of the 6 ROIs placed on the parenchyma liver are shown in figure 5: the 80 kVp series had the highest image noise. The iterative S5 protocols can be considered the best for noise reduction as they achieved the lowest noise both for DE reconstructions and 80 kVp. The iterative S5 80 kVp protocols had a noise lower than the standard FBP-B20 dual energy reconstruction.

![Noise liver parenchyma HU (SD)](image)

**Fig. 5:** Reconstruction noise

**References:** Department of Radiology, University of Brescia - Brescia/IT

**Detection Test**

The number of lesions detected for 80 kVp and DE_0.5 protocols are shown in table 6. Any significant difference between the number of lesions detected at 80 kVp and DE_0.5 series (ANOVA #=0.05) was observed. With the FBP-B20 kernel 2 / 32 subcentimeter low-contrast lesions were detected and the I30 S3, the second kernel used in routine protocol, permitted to identify 6 / 32. The average of lesions detected in all the strength-5 iterative kernels was 23 ± 1.2 / 32.
<table>
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<tr>
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<tr>
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<td></td>
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<td>19</td>
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<td></td>
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<td>I31S5 80 kV</td>
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Table 6:
Lesions detected by the 4 radiologists, out of 32: the sensitivity was higher with the most denoising kernels (S5), while the simulated subcentimeter lesions were almost undetectable with the standard FBP algorithm. (TP: true positive)

Fig. 6: Detection results

References: Department of Radiology, University of Brescia - Brescia/IT

Quality Test

The averaged results of the quality test are shown in table 7. The standard FBP-B20 and the I30 S3 kernels in the dual-energy series were the most appreciated by the 4 radiologist concerning the overall image quality (3.3 and 3.5 respectively), but there was not a statistically significant difference with others DE reconstructions, for example I30 S5 and I26 S3 (p > 0.05, ANOVA test).

All the 80 kVp series were rated as sub-optimal in terms of overall image quality (2.3 ± 0.3), sharpness (2.1 ± 0.4) and image noise (2.7 ± 0.2).

The series with both objective and subjective very low image noise, as DE_0.5 I26 S5, I31 S5, had a poor overall image quality score. An excessive reduction of the noise (3.8) led to a worsening of the structures sharpness (1.8).
Fig. 7: Quality test results

*References:* Department of Radiology, University of Brescia - Brescia/IT

*Images for this section:*
Figure 5:
Average values of the 6 ROIs placed on the liver parenchyma: the strength 5 series had a very low noise and so a higher contrast to noise ratio (CNR).

Fig. 5: Reconstruction noise
<table>
<thead>
<tr>
<th>TUBE A (80 kV)</th>
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<td>kernel</td>
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Lesions detected by the 4 radiologists, out of 32: the sensitivity was higher with the most denoising kernels (S5), while the simulated subcentimeter lesions were almost undetectable with the standard FBP algorithm. (TP: true positive)

Fig. 6: Detection results
Table 7:
Average results of the quality test: the standard FBP B20 was one the most appreciated kernels by the radiologists, but some iterative reconstruction had similar judgements. 80 Kv series had sub-optimal scores.

Fig. 7: Quality test results
Conclusion

Since the parameter "strength" is an additional degree of freedom to be tuned and it increases the possibilities of reconstructions, the protocol optimization with SAFIRE kernels could be difficult. In our study we attempted to determine the optimal DECT protocol that combine the detection with a familiar image appearance.

When iterative reconstructions (IR) are applied to the standard DE_0.5 acquisitions, there is a clear improvement in the detection of small low-contrast liver lesions. We demonstrated a great improvement in the sensitivity of a 6 mm lesion detection when the strength 5 is set. This protocol solution improves the sensitivity form 6% (FBP B20) to 75% (I30 S5).

It is important to underline that in our study we chose the most unfavorable conditions for the detection of lesions, because the diameter was sub-centimeter (6mm), the contrast was very low (+20 / +30 HU) and the image thickness was 2-mm. Despite this, the improvement of the sensitivity using the SAFIRE kernels was remarkable. That is, a SAFIRE kernel permitted the diagnosis of very low contrast lesions that would not be visible if images were reconstructed with the standard FBP algorithm. This greater sensitivity is mainly due to an improved physical image quality because of the strong noise reduction feature of strength 5 kernels.

However, the same kernels obtained a low acceptance by the subjective analyses. In fact, the radiologists tend to favour the standard FBP kernels. This discrepancy is related to the radiologists' "long" habit in referring patient's images reconstructed with standard FBP filters. As reported in many studies, Iterative reconstructions reduce noise and usually result in a different image texture. As a result images could be perceived as "different", not necessarily as "better" than the standard images. We believe that this side effect is mainly due to the short experience of radiologists with IR images. For these reasons, we think that the assessment of image quality for further protocol optimizations should be carried out through physical and clinical measurements in addition to subjective scores.

In our case, we identified the I26 S3 kernel as the most suitable to obtain the best image quality as it received a global score of 3.25 and the sensitivity was 68 % (22 / 32 simulated lesions); the I30 S5 kernel had the best sensitivity and a good quality ratings as well, but the images were too "plastic and pixellated".

We also explored a hypothetical low energy protocol using the data from the system A operating at 80 kVp. The main purpose in this analysis was to verify if a low energy acquisition could replace the standard DE acquisition in the arterial phase delivering half dose. The low-kVp series had a sensitivity similar to the DE_0.5 series but they were always rated as sub-optimal for the overall image quality. Therefore this low energy and low dose protocol cannot be used for a complete analysis and interpretation of the structures of the upper abdomen, even if images are reconstructed with the most
denoising SAFIRE kernels. It was confirmed that the 80 kVp image series allow the detection of hypervascular liver lesions with a very low contrast and small diameter, but others improvements in image quality are needed to use only a low energy CT scan for the study of the cirrhotic patients.

Concerning the optimization of the triphasic exams, a possible strategy could encompass a low tube voltage, half dose scan during the arterial phase and a standard 120 kVp scan for the other phases of the exam. If the kernel I31 S5 is used to reconstruct the arterial phase images, this acquisition could improve the sensitivity for hyper-dense liver lesions. The structures of the upper abdomen would be examined in an appropriate way in the precontrast- or portal-phases with a standard scan. This protocol would decrease the total dose of the exam of about 12%.

A greater dose reduction would be expected if the pre-contrast phase were replaced by a virtual non-contrast reconstruction obtained as a iodine subtraction to the DE acquisition. Some studies, however, showed that this is not possible yet and further improvement are needed to accurately "separate" contrast agent from calcifications [16].

We propose this including low-energy protocol for the arterial phase as a way towards dose saving and increase detection for CT exams of the abdomen as can be used on every scanner equipped with iterative reconstruction, like SAFIRE kernels, and with a sufficient tube current capabilities [17].

In conclusion, the SAFIRE reconstructions allow to detect a higher number of simulated hypervascular liver lesions compared to the standard reconstructions, even with an 80-kVp protocol. According to our data, a single low tube voltage acquisition protocol is not sufficient yet because of the sub-optimal image quality.
Figure 8:
Arterial phase scan of a hyper enhanced lesion of the liver, reconstructed with 3 different kernels.

**Fig. 8:** Different kernels

**References:** Department of Radiology, University of Brescia - Brescia/IT

**Images for this section:**
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**Fig. 8:** Different kernels
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