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COMPUTED TOMOGRAPHY

Dual-energy CT for liver iron quantification in patients with haematological disorders

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Abstract

Objectives To retrospectively quantify liver iron content in haematological patients suspected of transfusional haemosiderosis using dual-energy CT (DECT) and correlate with serum ferritin levels and estimated quantity of transfused iron.

Methods One hundred forty-seven consecutive dual-source dual-energy non-contrast chest-CTs in 110 haematologic patients intended primarily for exclusion of pulmonary infection between September 2016 and June 2017 were retrospectively evaluated. Image data was post-processed with a software prototype. After material decomposition, an iron enhancement map was created and freehand ROIs were drawn including most of the partially examined liver. The virtual iron content (VIC) was calculated and expressed in milligram/millilitre. VIC was correlated with serum ferritin and estimated amount of transfused iron. Scans of patients who had not received blood products were considered controls.

Results Forty-eight (32.7%) cases (controls) had not received any blood transfusions whereas 67.3% had received one transfusion or more. Median serum ferritin and VIC were 138.0 μg/dl (range, 6.0–2628.0 μg/dl) and 1.33 mg/ml (range, − 0.94–7.56 mg/ml) in the post-transfusional group and 27.0 μg/dl (range, 1.0–248.0 μg/dl) and 0.61 mg/ml (range, − 2.1–2.4) in the control group. Correlation between serum ferritin and VIC was strong ($r = 0.623$; $p < 0.001$) as well as that between serum ferritin and estimated quantity of transfused iron ($r = 0.681$; $p < 0.001$).

Conclusions Hepatic VIC obtained via dual-energy chest-CT examinational protocol strongly correlates with serum ferritin levels and estimated amount of transfused iron and could therefore be used in the routine diagnosis for complementary evaluation of transfusional haemosiderosis.

Key Points

- *Virtual liver iron content was measured in routine chest-CTs of haematological patients suspected of having iron overload. Chest-CTs were primarily intended for exclusion of pulmonary infection.*
- *Measurements correlate strongly with the most widely used blood marker of iron overload serum ferritin (after exclusion of infection) and the amount of transfused iron.*
- *Liver VIC could be used for supplemental evaluation of transfusional haemosiderosis in haematological patients.*

Keywords Tomography, X-ray computed · Haemosiderosis · Erythrocyte transfusion · Haematologic diseases · Liver

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Abbreviations

DE	Dual-energy
DECT	Dual-energy computed tomography
IQR	Interquartile range
LIC	Liver iron content
RBC	Red blood cells
SD	Standard deviation
VIC	Virtual iron content

Introduction

Patients with haematological disorders frequently develop anaemia either directly caused by the underlying disease (e.g. leukaemia, myelodysplastic syndrome, other types of anaemia) or secondary during cytotoxic chemotherapy [1]. Supportive care typically includes blood transfusions, either to bridge phases of aplasia or as a continuous and repeated means of treatment in the palliative setting. Depending on the magnitude and duration of iron administration through blood transfusions, increased parenchymal storage of iron in the liver and other organs is expected [2]. A unit of packed red blood cells (RBC) contains approximately 200–220 mg of iron. Thus due to limited iron excretion in humans, the body's iron content increases with each RBC transfusion [3]. The liver is the major site of iron storage in iron overload with about 70% of total body iron [3, 4]. Nevertheless, contrary to hereditary hemochromatosis, in cases of secondary transfusion-related iron overload, iron is first deposited in the bone marrow and spleen before other organs become involved [3]. This form of iron overload is generally called transfusional haemosiderosis and is frequently encountered in haematological patients [5, 6]. The normal liver iron content is < 1.8 mg Fe/g dry tissue [7]. With increasing liver iron concentration, liver dysfunction as well as structural changes up to liver fibrosis and cirrhosis are expected, and the incidence of other morbidities including vascular, endocrine and osseous increases [8]. For this reason, accurate assessment of the liver iron content is imperative with growing interest for non-invasive techniques substituting liver biopsy [9]. The role of ferritin quantification in plasma or serum has been highlighted by numerous previous reports and this approach has become the most frequently used test applied in the routine diagnosis of haemosiderosis. However, ferritin is a surrogate marker of iron stores as well as an acute-phase reactant. Especially infections, which are quite common in haematological patients, regularly induce falsely high ferritin levels. An alternative estimate is represented by the quantification of iron contained in administered RBCs using different formulas [3].

In the last decades, various MRI-based techniques have been shown to be able to provide adequate quantification of liver iron [10]. With the advent of the dual-energy CT technique and related DE-based material decomposition, CT has evolved into an alternative to MRI for quantifying tissue iron being more easily accessible and providing shorter examination times [11]. Moreover, chest-CT is frequently used in haematological patients in particular during the long immunosuppression period after bone marrow transplantation for exclusion of pulmonary infections and non-infectious complications. Besides representing the most sensitive imaging technique in this clinical scenario, these CT scans display parts of the liver and spleen.

The current CT study aims at quantifying liver iron content in routine chest-CTs using DECT technology and a dedicated post-processing prototype proving its applicability in the routine diagnosis providing valuable add-on information. As standard-of-reference, both serum ferritin (after exclusion of all cases suspected of concurrent infection) and the estimated amount of administered iron were used.

Material and methods

Patient population

This retrospective data evaluation was approved by the institutional review board (registration number 590/2017B02). Verbal informed consent was obtained from all patients. The CT examinational protocol was standard-of-care at our institution for non-contrast chest-CT since July 2016. We retrospectively identified 272 consecutive CT scans acquired between September 2016 and June 2017 in 152 (median age 61.8 years; range 18.6–88.8; 63 (41.4%) female, 89 (58.6%) male) haematological patients. Chest-CT examinations were part of the routine work-up in these patients performed primarily for exclusion of pulmonary infection during or before institution of antitumor treatment. Cases with an elevated CRP > 4 mg/dl as well as clinical or radiological evidence of infection at the time of serum ferritin quantification (42 patients and a total of 125 CT examinations) were excluded in order to avoid cases of elevated serum ferritin values related to ferritin's properties as an acute phase reactant. Furthermore, we excluded cases with known liver pathology (active form of hepatitis, cirrhosis, status post liver transplantation, hepatic manifestations of underlying disease), cases in which the patient had received chelation therapy during the previous 6 months and cases without corresponding ferritin value. One hundred forty-seven CT scans of 110 (median age 60.1 years, range 18.6–80.6 y; 47 (42.7%) female, 63 (57.3%) male) patients examined between September 2016 and June 2017 were finally included in this study. All patients underwent serum ferritin measurements close (median 0.0 days; range − 42–78 d) to the DECT examination, the former being part of a standardised laboratory work-up of haematological patients at our institution. Data regarding the number of blood transfusions received in each case during the 6-month period before the CT examination was obtained from

the local blood bank and the estimated amount of transfused iron was calculated using the currently recommended formula [12]. Earlier blood transfusions were historically excluded. In 99 cases (67.3%), the patient had received blood transfusions (mean, 10.0; range 1–56) whereas in 48 cases (32.7%), the patient had not. The latter subgroup represents our control cohort. The underlying haematological disorders were as follows: acute myeloid leukaemia ($n = 57$), myelodysplastic syndrome/myeloproliferative neoplasia ($n = 22$), acute lymphoblastic leukaemia ($n = 10$), chronic myelomonocytic leukaemia ($n = 9$), multiple myeloma ($n = 7$), chronic myeloid leukaemia ($n = 4$), T-lymphoblastic lymphoma ($n = 3$), severe aplastic anaemia/very severe aplastic anaemia ($n = 4$), severe combined immunodeficiency ($n = 2$), chronic lymphocytic leukaemia ($n = 2$), toxic pancytopenia ($n = 1$), Waldenström's disease ($n = 1$), idiopathic myelofibrosis ($n = 1$), follicular lymphoma ($n = 1$), diffuse large B cell lymphoma ($n = 1$), acquired haemophilia A ($n = 1$), and Evan's syndrome ($n = 1$). Forty-eight cases with no history of blood transfusions were used as a control group. Haematologic patients in this group did not suffer from MDS or anaemia, disorders that may be associated with ineffective erythropoiesis or increased intestinal iron absorption. A group of non-haematologic cases ($n = 19$) was included in the controls.

CT acquisition

All CT examinations were performed with the same 2 × 128-slice DECT scanner (SOMATOM Definition Flash, Siemens Healthineers). The examinational protocol used dual-energy (DE, 100 and 140kVp) with a tin filter to improve separation of the two energy spectra. The effective tube currents were 89 mAs and 76 mAs with 0.28 s rotation time, pitch 0.7, 64 × 0.6 acquisition, 512 × 512 matrix, 1.5 mm slice thickness, 1 mm increment, medium smooth Q30f kernel and iterative reconstruction (i3). The upper half of the liver was scanned as part of this chest imaging protocol.

CT data analysis

Image data was post-processed with a software prototype on a dedicated research workstation (DE IronVNC; syngo.via Frontier; Siemens Healthineers). A liver map was created using base material decomposition into air, water and iron. Two radiologists (H.M. and W.S.) with 25 and 2 years of experience in CT diagnosis performed joint image analysis. Virtual iron content (VIC) of the liver was measured by placing three large freehand ROIs, while leaving approximately 1 cm at the dome of the liver as well as along the liver capsule excluding also larger vessels in the vicinity of the portal and inferior caval veins. The ROIs included the left liver lobe and the anterior part of the right liver lobe. The VIC expressed in milligram/millilitre was subsequently obtained from the ROI tool. Median ROI size was 49.7 cm^2 (range, 13.3–144.8 cm^2). Additionally, a second freehand ROI was measured on each of the three consecutive slices in corresponding fashion encompassing the whole liver including the posterior part of the right lobe. Median ROI size was 111.9 cm^2 (range, 49.0–244.0 cm^2). The measurements of VIC were averaged. ROI quantification provided iron concentration as well as iron enhancement in Hounsfield units (HU) at an equivalent X-ray tube voltage of 120 kV.

Laboratory parameters and estimated transfusion-associated iron load

The central laboratory of our institution classifies serum ferritin levels > 20 μg/dL in women and > 30 μg/dL in men as pathological. To divide the patient population into subgroups, we used cutoff values of 100 μg/dL and 250 μg/dL since they are used as cutoff values in iron chelation therapy according to various guidelines [13].

The number of RBC transfusions during the 6 months prior to the respective CT scan was obtained from the local blood bank. Subsequently, the estimated total iron content of administered blood products was calculated for each patient using the following formula:

$$\text{Amount of transfused iron } (g) = Hb\ (14\ g/dL) \times 0.5\ L \times 0.0034 \times \text{number of RBC transfusions}$$

Haemoglobin (Hb) of 14 g/dL was estimated under the following assumptions: at the local blood bank, each RBC concentrate contains erythrocytes from 500 mL of donor blood. Eligibility for donation requires a minimum Hb of 12.5 g/dL for women and 13.5 g/dL for men and is rarely greater than 15 g/dL resulting in an estimated mean Hb of 14 g/L. The factor 0.0034 represents the amount of 3.4 mg of iron per 1 g of haemoglobin [12].

Statistical analysis

Correlations between VIC, serum ferritin and the amount of transfused iron were assessed by using Spearman correlation analysis for non-normal distribution data. To address dependence of CT scans within patients, we also performed correlation analysis for the following subgroups: (1) subgroup including only primary CT scans, excluding additional CT scans in patients with multiple exams, (2) subgroup including only exams of patients that received only one CT scan and (3) subgroup including only exams of patients who received multiple CT scans.

Differences regarding the level of VIC and serum ferritin between groups were assessed using the Kruskal–Wallis test

and the Mann–Whitney *U* test. To address multiple comparisons, the Bonferroni correction was applied: in case of comparison of three different groups, i.e. three tests, a *p* value of 0.016 was considered significant. In case of comparison of four different groups, i.e. six tests, a *p* value of 0.008 was considered significant. These *p* values were determined by dividing the standard *p* value of 0.05 by the number of tests in the respective comparison.

Differences regarding VIC between ROI measurements excluding the posterior part of the right liver lobe and ROI measurements including the whole liver were assessed using the Wilcoxon signed-rank test for related samples.

Statistical analysis was performed by using software (IBM SPSS Statistics Version 22). $P < 0.05$ was indicative of a statistically significant difference.

Results

Transfusion subgroup

In the group of patients receiving blood transfusions, the median estimated cumulative amount of transfused iron was 2.38 g (IQR, 3.57; range, 0.2–13.3 g). The median number of blood transfusions was 10.0 (IQR, 15.0; range, 1–56).

The median serum ferritin concentration was 138.0 μg/dL (IQR, 176.0; range, 6–2628 μg/dL).

The calculated median VIC was 1.33 mg/mL (IQR, 1.17; range, − 0.94–7.56).

Using the Kruskal–Wallis test to determine differences between multiple groups there were significant differences regarding VIC and serum ferritin between those patients with 0, 1–10, 11–20 or > 20 blood transfusions ($p < 0.001$). When comparing each of the groups separately using the Mann–Whitney *U* test, no significant differences were found regarding VIC when comparing patients with 1–10 and 11–20 transfusions ($p = 0.095$) and regarding serum ferritin when comparing patients with 11–20 and > 20 transfusions ($p = 0.021$; Tables 1 and 2).

Controls

The median serum ferritin value was 27.0 μg/dL (IQR, 70.0). The calculated median VIC was 0.61 mg/mL (IQR, 0.86) (Tables 1 and 2).

Correlations between VIC, serum ferritin and amount of transfused iron

An overview over the correlation analysis is given in Table 3.

When considering all exams, the correlation between VIC and serum ferritin was strong ($r = 0.623$; $p < 0.001$; Fig. 1), as well as the correlation between serum ferritin and the number of received blood transfusions ($r = 0.681$; $p < 0.001$; Fig. 2). The correlation between VIC and the number of transfusions, i.e. transfused amount of iron was $r = 0.558$ ($p < 0.001$; Fig. 3). After exclusion of an extreme outlier, positive correlation between serum ferritin and hepatic VIC as well as between serum ferritin yielded $r = 0.616$ ($p < 0.001$). The outlier is a 53-year-old male patient with chronic myelogenous leukaemia, a long history of blood transfusions ($n = 56$ during the previous 6 months) and showed an exceptionally high serum ferritin of 2628 μg/dL and a mean measured liver VIC of 7.56 mg/ml (Fig. 4)

Regarding only exams from patients that had received blood transfusions, the correlations between VIC and serum ferritin, between serum ferritin and the number of transfusions and between VIC and the number of transfusions were $r = 0.544$ ($p < 0.001$), 0.519 ($p < 0.001$) and 0.488 ($p < 0.001$), respectively. Regarding the control group, the correlation between VIC and serum ferritin was $r = 0.476$ ($p = 0.001$).

The correlation between liver VIC and serum ferritin in the subgroup including all primary CT scans excluding additional CT scans in patients with multiple exams ($n = 110$) was $r = 0.629$ ($p = 0.000$). For the subgroup including only exams of patients that received only one CT scan ($n = 85$), the correlation was $r = 0.622$ ($p = 0.000$). For the subgroup including only exams of patients who received multiple CT scans ($n = 62$), the correlation was $r = 0.580$ ($p = 0.000$).

Performance of VIC based on grading of serum ferritin values

There were significant differences regarding VIC in those patients with serum ferritin levels of 0–100 μg/dl, 101–250 μg/dl and > 250 μg/dl as assessed by the Kruskal–Wallis test ($p < 0.001$). Comparing the subgroups separately using the Mann–Whitney *U* test also yielded a significant difference for each comparison ($p < 0.002$) (Table 1).

Spatial distribution of VIC within the liver

The calculated median VIC values obtained with the additionally measured ROI, including the posterior part of the right liver lobe, were 0.61 mg/dL for all cases, 1.17 mg/dL for patients who received blood transfusions and 0.33 mg/dL for the control group, i.e. significantly lower compared to ROI measurements excluding the posterior part of the right lobe which were 1.11 mg/dL, 1.33 mg/dL and 0.61 mg/dL, respectively ($p < 0.001$).

Discussion

Our results show that the VIC of the liver strongly correlates with both serum ferritin values and the quantity of transfused iron. We found also good correlation between serum ferritin and the amount of transfused iron in support of the use of the former as a surrogate parameter in patients suspected of post-transfusional

Table 1 Hepatic VIC values (mg/mL) for all cases, cases that received blood transfusions, control cases and subgroups (regarding serum ferritin levels and number of transfusions) of cases that received transfusions

		Number	Median	IQR	Min.	Max.
All cases		147	1.11	1.11	− 2.05	7.56
Received transfusions		99	1.33	1.17	− 0.94	7.56
Controls		48	0.61	0.86	− 2.05	2.44
Received transfusions	0–100 μg/dl	34	1.08	0.77	− 0.94	1.84
	101–250 μg/dl	40	1.31	1.22	− 0.39	5.22
	> 250 μg/dl	25	2.06	1.44	0.44	7.56
	1–10 transfusions	52	1.08	0.86	− 0.94	3.11
	11–20 transfusions	25	1.33	1.33	0.00	4.72
	> 20 transfusions	22	2.47	1.50	1.44	7.56

haemosiderosis, i.e. accumulation of iron in the liver. In order to exclude potential ferritin-related bias, we deliberately obviated patients with evident signs of infection from the final calculation.

Hence, the aim of this project was to explore the potential of a routine CT examinational protocol, intended primarily to exclude pulmonary infection in patients with haematological diseases, for delivering add-on information about the liver iron content. The rationale of this approach is based on the knowledge that accumulation of iron in the liver parenchyma will lead to a much stronger increase in CT values in the low kV images than in the high kV images (in the absence of additional X-ray filtration approximately 50% more at 80 kV) [14]. This difference can be exploited to perform a material decomposition into water and iron and consequently to calculate the iron enhancement in the image. Base material decomposition provides iron concentration in terms of milligram/millilitre which can be converted with help of a known conversion factor to conventional LIC (liver iron content) expressed in milligram/gram dry tissue [15]. As the X-ray attenuation of iron is different from iodine contrast agent, the detection threshold for iron is higher than for iodine and appears to be approximately 2.3 mg/mL [11]. Earlier attempts of liver iron quantification using single energy technique proved less accurate for iron concentrations below 15–20 mg/g dry weight compared to MRI and inaccurate for LIC < 8 mg/g dry weight [3, 16]. According to Wood et al [3], intersubjective variability in intrinsic liver attenuation was the major limitation and the dominant source of measurement uncertainty. This result can probably be explained by the natural spread of CT values of human liver parenchyma even in the absence of iron, which is caused by confounding effects like liver fat or food intake prior to the examination [17].

More recent reports by Fischer et al demonstrated in an ex vivo phantom study that DECT using dedicated iron-specific 3-material decomposition accurately quantifies liver iron contents as low as 20 μmol/g regardless of the liver fat content and that the latter can be quantified even in the presence of both hepatic iron and iodinate contrast agents [18, 19]. Interestingly, in our series we could quantify VIC even in controls where measured ferritin values were significantly lower compared to haemosiderosis patients lying close to or within the accepted normal values. However, even the currently accepted normal ranges for serum ferritin vary considerably between 20 and 50 μg/dl [20, 21].

In order to find out how good this technique works depending on the degree of transfusional hepatic iron accumulation, we performed separate statistics in patients with different magnitudes of serum ferritin and amounts of transfused iron. This comparison yielded significant differences regarding VIC values depending on the ferritin level classes (0–100 vs. 101–250 vs. > 250 μg/L). At the same time, our results showed good correlation between VIC and the number of blood transfusions, i.e. the amount of transfused iron. However, within closer ranges (1–

Table 2 Serum ferritin values (μg/dL) for all cases, cases that received blood transfusions, control cases and subgroups (regarding serum ferritin levels and number of transfusions) of cases that received transfusions

		Number	Median	IQR	Min.	Max.
All cases		147	99.00	156.00	1.00	2628.00
Received transfusions		99	138.00	176.00	6.00	2628.00
Controls		48	27.00	70.00	1.00	248.00
Received transfusions	0–100 μg/dl	34	61.50	33.00	6.00	99.00
	101–250 μg/dl	40	145.00	66.50	106.00	239.00
	>250 μg/dl	25	394.00	241.00	252.00	2628.00
	1–10 transfusions	52	90.00	90.50	6.00	652.00
	11–20 transfusions	25	145.00	130.00	53.00	729.00
	> 20 transfusions	22	247.50	360.00	66.00	2628.00

Table 3 Correlations between liver VIC, number of RBCs and serum ferritin for all exams and different subgroups

Subgroup	Number of exams	Variables	Spearman's rho	*p* value
All exams	147	Liver VIC/serum ferritin	0.623	0.000
		Liver VIC/number of RBCs	0.558	0.000
		Serum ferritin/number of RBCs	0.681	0.000
Received transfusions	99	Liver VIC/serum ferritin	0.544	0.000
		Liver VIC/number of RBCs	0.488	0.000
		Serum ferritin/number of RBCs	0.519	0.000
Controls	48	Liver VIC/serum ferritin	0.476	0.001
Primary CT scans	110	Liver VIC/serum ferritin	0.629	0.000
Single CT scans	85	Liver VIC/serum ferritin	0.622	0.000
Multiple CT scans	62	Liver VIC/serum ferritin	0.580	0.000

10 vs. 11–20 blood transfusions), the difference in VIC between groups did not reach statistical significance. In the report by Joe et al, the difference (ΔH) of averaged attenuation between 80 and 140 kV at CT significantly correlated with the degree of iron concentration in the phantom arm of their study [22]. Moreover, DECT performed comparable with MRI in this study reaching a correlation coefficient > 0.8 for both techniques and therefore the authors concluded that this technique was accurate for the diagnosis of clinically important haemosiderosis. However, in the human arm, correlation between ΔH and the quantitative amount of iron was lower in patients who had less than 10% iron according to histopathology. Generally, correlations between non-invasive quantification of liver iron and histologic probes of human or animal livers yielded better results as

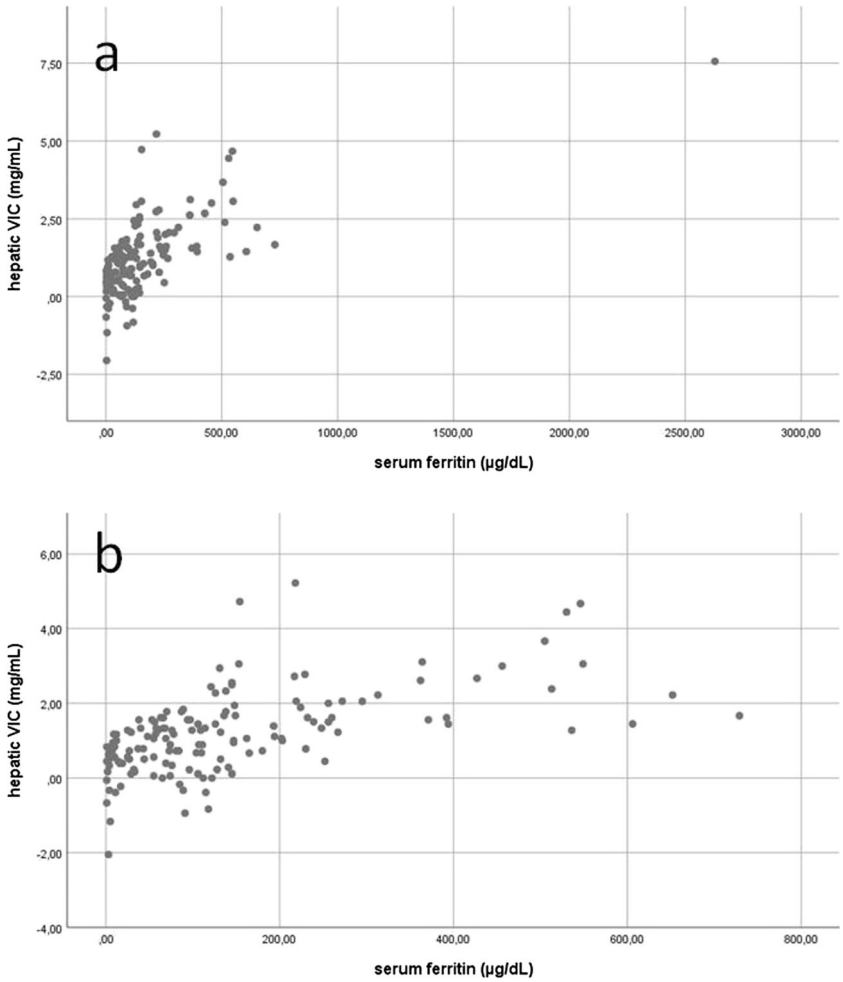

Fig. 1 Correlation between serum ferritin and hepatic VIC before and after exclusion of one outlier. **a** Scatterplots show positive correlation between serum ferritin and hepatic ($r = 0.623$, $p < 0.001$). **b** After the exclusion of one outlier presenting with exceptionally high serum ferritin correlation is $r = 0.616$ ($p < 0.001$)

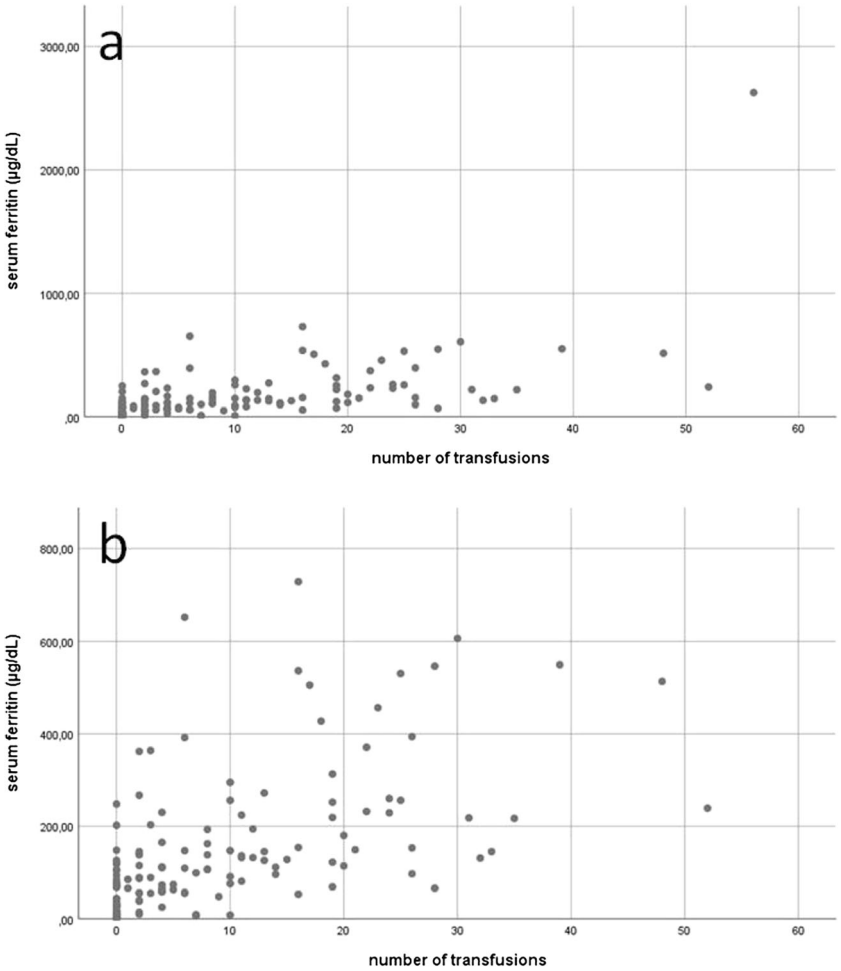

Fig. 2 Correlation between serum ferritin and number of blood transfusions before and after exclusion of one outlier. **a** Scatterplots show positive correlation between serum ferritin and number of blood transfusions for all cases ($r = 0.681$, $p < 0.001$). **b** After the exclusion of one outlier correlation is $r = 0.674$ ($p < 0.001$)

compared to reports using serum ferritin as a marker for liver haemosiderosis [22–25]. This probably also explains the significantly better correlation between VIC quantification based on DE technique and those obtained using R2* MRI technique [11] as compared to the reported correlations with serum ferritin.

Notably, our retrospective analysis yielded strong but not perfect correlation between VIC and ferritin. The standard deviation of the virtual iron concentration in our control group indicates that the typical measurement error of the dual-energy method is 1.1 mg/mL or less, while the baseline can be as high as 1.1 mg/mL. It is difficult to provide more precise numbers, as there was some liver iron content also in the control group. A recent study by Kühn et al [26] that measured liver iron content with the R2* technique in a large German population-based cohort found a prevalence of 17.4% for hepatic iron overload. Since dual-energy CT is a linear method, it is expected that there is also a similar measurement error for small, non-zero iron concentration. The observed higher IQR for the higher serum ferritin bins as well as for the higher number of transfusions is therefore at least partly related to the spread of iron concenrations within each bin. In our cohort, most VIC values were crowded within the lower serum ferritin ranges as most patients had only temporarily received blood transfusions (before and during chemotherapy with allogeneic stem cell transplantation). However, correlations between VIC/hepatic attenuation (HU) and serum ferritin levels remained consistent even after excluding an outlier (a patient with chronic myelogenous leukaemia and a long history of repeated 56 blood transfusions) presenting with extremely high VIC and serum ferritin values. The same was true also with respect to the correlation of serum ferritin levels and the number of transfusions/amount of administered iron. To address dependence of CT scans within some of the patients we also performed correlation analysis for the following subgroups: (1) subgroup including only primary CT scans, excluding additional CT scans in patients with multiple exams, (2) subgroup including only exams of patients that received only one CT scan and (3) subgroup including only exams of patients who received multiple CT scans. This additional analysis yielded similar correlations and shows that dependence of scans within subjects was not a problem in our cohort.

Recently, dual-source CT was used to determine the spatial distribution of iron within the normal human liver yielding higher iron concentrations in the middle-to-upper part of the liver, medially and anteriorly [27]. These data are in line with

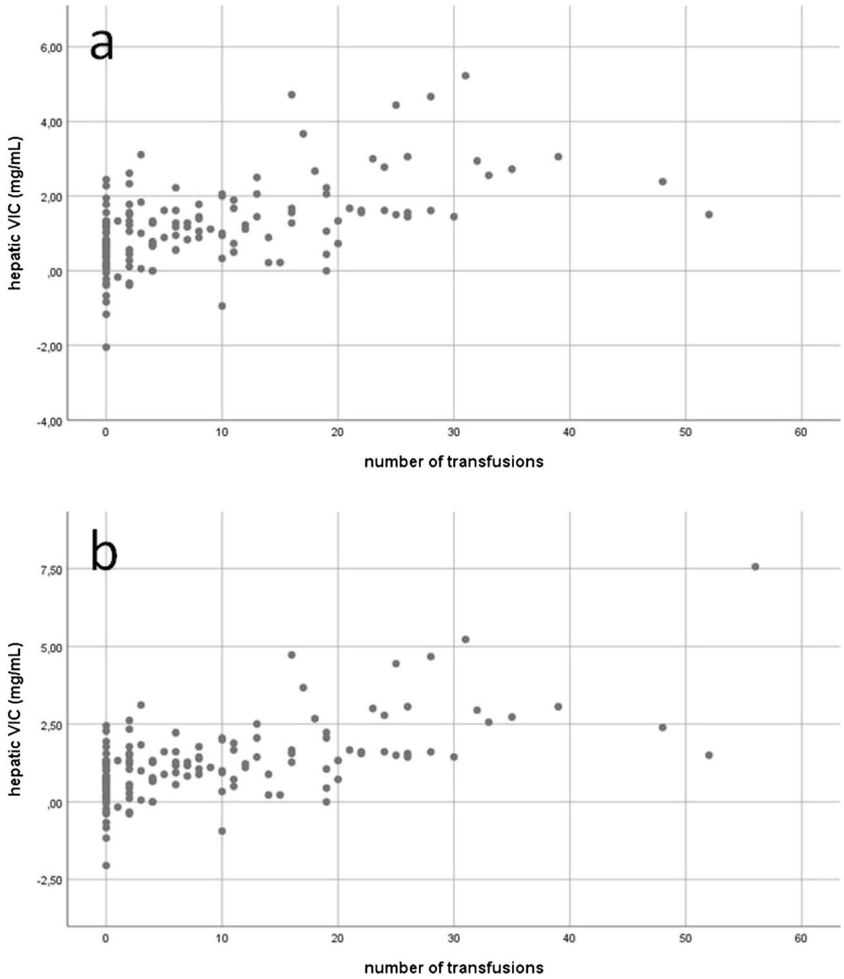

Fig. 3 Correlation between hepatic VIC and the number of blood transfusions before and after the exclusion of one outlier. **b** Scatterplots show positive correlation between hepatic VIC and the number of blood transfusions ($r = 0.558$, $p < 0.001$). **a** After the exclusion of one outlier correlation is $r = 0.549$ ($p < 0.001$)

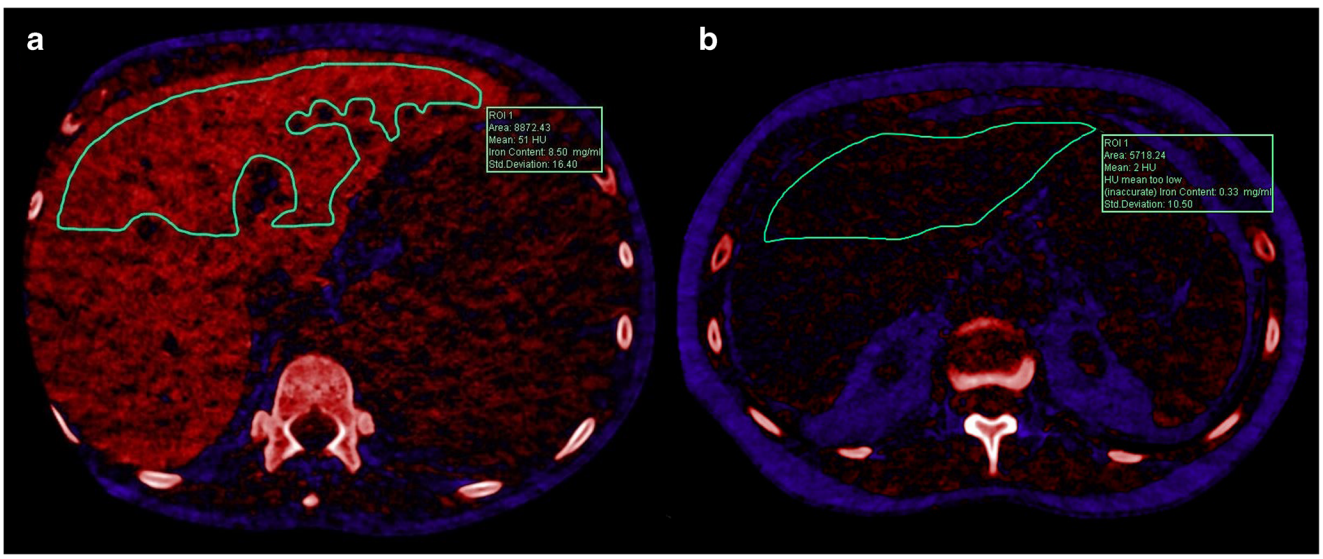

Fig. 4 Example cases of elevated and normal liver iron showing ROI placement in liver VIC map. **a** 53-year-old male with chronic myelogenous leukaemia, long history of blood transfusions ($n = 56$ during previous 6 months) and an exceptionally high serum ferritin of 2628 μg/dL. Measured liver VIC is 8.50 mg/mL. **b** 63 year old female with first diagnosis of secondary myelodysplastic syndrome, no history of blood transfusion and a normal serum ferritin of 3.1 μg/dL. Measured liver VIC is 0.33 mg/mL

our own results which also showed slightly higher VIC when excluding the posterior parts of the liver parenchyma. A possible explanation for this phenomenon could reside in lower measurement accuracy close to the spine due to beam hardening artefacts in particular in case of using lower energy levels. However, contrary to sampling bias at liver biopsy due to spatial heterogeneity of tissue iron deposition (e.g. in coexisting fibrosis), the use of multiple large ROIs is expected to overcome this limitation [28, 29].

This project was not meant to compete against MRI-based liver iron quantification, but to offer a new possibility of getting valuable add-on information in a one-stop shop fashion in a frequent clinical setting where haematologic patients suspected of both pulmonary complications and post-transfusional haemosiderosis undergo routine unenhanced chest-CT examinations. Nevertheless, this technique could also primarily be applied for liver iron evaluation.

This study has some limitations. First, iron quantification could not be performed in the whole liver, but in the upper half as we retrospectively evaluated chest-CT data. Second, we did not have histologic correlation to our data, but used serum ferritin values and the estimated quantity of transfused iron as a standard of reference. Third, the serum ferritin levels in our cohort were representative only for cases with low to moderate liver iron deposition, but this seems to be actually more significant in the clinical setting that was addressed in this paper.

Conclusion

In conclusion, hepatic VIC determined based on non-contrast routine DECT image data obtained with a routine examinational protocol and calculated with the proposed post-processing prototype shows strong correlation with serum ferritin and the amount of transfused iron and could therefore be used in the daily routine diagnosis for complementary evaluation of transfusional haemosiderosis.

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Compliance with ethical standards

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Conflict of interest Bernhard Krauss is an employee of Siemens Healthcare GmbH, Diagnostic Imaging, Computed Tomography, Scanner Applications, HC DI CT R&D CTC SA, Siemensstr. 3, 91301 Forchheim, Germany.

Ulrike Haberland is an employee of Siemens Healthcare Limited, HC WEA GBR DI PI, Sir William Siemens Square, Frimley, Camberley GU16 8QD, UK.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Cross sectional study
- Performed at one institution

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