Expert Input

The survey was sent out to over 200 clinicians and specialist nurses, including Late Effects Clinic Directors, Oncologists, and Haematologists. The results contained in this report were collated from 33 respondents across 11 centres of excellence, treating over 670 patients between them. The survey response was excellent and as such is considered a valid snapshot of current practice.

Following the publication of several studies discussing the occurrence of transfusional iron overload in cancer survivors, Resonance Health asked specialist healthcare providers to complete a survey on clinical practice in monitoring and treating iron overload in this cohort. There were over 30 respondents from the UK, US, and Germany, including Clinicians, Specialist Nurses, and other healthcare providers.

With the effects of iron overload in haemoglobinopathies such as Thalassemia and Sickle Cell Disease well documented, concerns are now being raised about the incidence of transfusional iron overload in cancer survivors. Currently monitoring for iron overload is mentioned in some cancer survivorship guidelines but is noticeably absent from others. This report presents the findings from a survey of experts in the treatment of cancer on current clinical practice across various centres and countries and reveals the variations in current screening and treatment practice and highlights the need for improved iron monitoring.
Survey Participants

Over 90% of respondents were clinicians, 6% were specialist nurses, and 3% fell into the ‘Other’ category. Respondents were asked a variety of questions about current clinical practices in screening for and treatment of iron overload in their cancer survivor patients.

Summary of Results

How many patients received transfusions or iron supplements as part of their cancer therapy?

Over 42% had 20 or more patients each year receiving transfusions or supplementary iron as part of their cancer therapy.

What percentage of cancer survivors have received more than 10 transfusions and maybe at risk of transfusional iron overload?

27% of respondents estimated that 10-20% of their patients had received more than 10 transfusions as part of their treatment.

24% estimated that this percentage was 20-40% of their patients.

24% of respondents estimated that 40-60% of their patients had received more than 10 transfusions as part of their treatment.

As a weighted average, this amounts to approximately 24% of patients who receive more than 10 transfusions.
Which disease cohort requires the most transfusions thereby putting them at most risk of transfusional iron overload?

Results indicated that transfusion was used across multiple disease cohorts, however those patients undergoing hematopoietic stem cell transplantation (HSCT) required the most transfusions, followed by the acute myeloid leukemia (AML) patient group then the myelodysplastic syndrome (MDS) group.

How are iron levels in cancer survivors being monitored?

Techniques for monitoring of iron levels varied between respondents. Whilst recent opinion cautions against reliance on serum ferritin as an accurate indicator of body iron stores, over 70% of clinicians used regular blood tests (serum ferritin) as an indicator of iron overload. The majority (65%) use a cutoff level of >1000ng/mL at which further action is required. Interestingly 12.5% used >1500ng/mL and a further 12.5% used >500ng/mL, so there is widespread variability amongst caregivers as to the most appropriate cutoff level. Nearly 40% of respondents use FerriScan to measure liver iron concentration in cancer survivors at risk.

Barriers to optimal iron monitoring in cancer survivors using FerriScan?

69% of respondents stated the lack of guidelines on the use of quantitative MRI measurement of iron overload in cancer survivors was a challenge to the use of FerriScan. The other major barrier to using FerriScan is a lack of funding for performing an MRI for liver iron concentration (19% described this as a minor challenge, 41% described this as a significant challenge). Interestingly, 44% of respondents thought that the perception that other tests, such as serum ferritin and liver biopsy, were more suitable was not a barrier to using FerriScan.

Could iron monitoring be improved at centres treating cancer survivors?

93% of respondents thought that iron monitoring practices could be improved at their centre.
Treatment methods for patients in whom iron overload is detected

Results showed treatment of patients identified with iron overload was widely varied, as the following column graph details. This variability exists both between healthcare providers and within healthcare providers’ patient groups.

Call for information and further local screening using FerriScan for cancer survivors

62% of respondents expressed interest to participate in an iron monitoring audit using FerriScan. 40% desired collaboration with other FerriScan centres to improve iron monitoring and establish guidelines, and over 50% requested further information.
Key Conclusions

- The clinical survey showed that a significant percentage of cancer survivors treated by these respondents were exposed to transfusional iron overload. Almost half of respondents said at least 20% of their cancer survivors had received over 10 transfusions.

- There is a widespread call amongst these clinicians for more information and guidance on iron monitoring and management in cancer survivors. This is supported by participants’ perception that lack of guidelines alongside funding is a current challenge to optimal iron monitoring in this cohort.

- An overwhelming 93% of survey participants indicated that iron monitoring could be improved at their centre and the majority indicated they would like to participate in a local screening program using FerriScan to better identify and treat patients at risk. There is a strong desire for collaborations between centres on this. As FerriScan is the Gold Standard measurement for Liver Iron Concentration, regulatory cleared, and standardised, there may be immediate opportunities for a FerriScan information network to advance health outcomes in this area.

- Resonance Health will continue to engage and partner with the clinical community to add value to local screening programs. Wherever possible we will promote the use and benefits of FerriScan and facilitate collaborations between centres to assist in the management of potential iron toxicity and late effects in this vulnerable patient cohort. As serum ferritin is an acute phase reactant, using it as a measure of liver iron concentration may not be as accurate as required and recent opinion cautions against reliance on it.

For further information or to request your local FerriScan audit pack – please contact Alison Laws at alisonl@resonancehealth.com.

Thank you very much to all those who participated in the survey.
Serum ferritin and FerriScan in clinical management of iron overload in pediatric cancer survivors

Case Study 1: A 17 year old male with neuroblastoma (diagnosed at 2 years of age) subsequently had a bone marrow transplant (BMT) as part of his multi-modal treatment plan. Four years after his BMT, the serum ferritin (SF) measurement was 2991 microg/L. Given his high SF, he was subsequently phlebotomised for just over 2 years at which time his SF was reduced to 631 microg/L. A FerriScan measurement was also made at this time. At a level well below the commonly used SF screening threshold of 1000 microg/L, this survivor had a liver iron concentration (LIC) of 9 mg Fe/g, indicating he was still above the LIC threshold of 7 mg Fe/g where iron overload is still a concern. With the certainty and confidence FerriScan provided, phlebotomy treatment was therefore continued for another 2 years until his LIC returned to normal (2 mg Fe/g).

<table>
<thead>
<tr>
<th>Average Liver Iron Concentration</th>
<th>9.0 mg/g dry tissue <em>(NR: 0.17-1.8)</em></th>
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<tr>
<td></td>
<td>160 mmol/kg dry tissue <em>(NR: 3-33)</em></td>
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Normal range (NR) is taken from Bassett et al., *Hepatology* 1986; 6: 24-29.

![Graph showing liver iron concentration with Transverse Relaxation Rate (R2) Image and Transverse Relaxation Rate (R2) Distribution](image-url)
Case Study 2: A 19 year old female with juvenile myelomonocytic leukemia (diagnosed at 5 years of age) received a bone marrow transplant (BMT) as part of her treatment. Her serum ferritin (SF) level seven years after treatment was 2189 microg/L and her liver iron concentration (LIC) was 18.6 mg Fe/g. Owing to her obvious iron overload she underwent phlebotomy treatment. After 30 months of regular treatment her SF had been reduced to 727 microg/L, but her LIC was still 6.6 mg Fe/g and so treatment was continued. Two years later her SF was 1187 microg/L, but had been consistently below 1000 microg/L in the previous two years. A FerriScan 2 months later returned an LIC of 1.5 mg Fe/g indicating her LIC had returned to normal levels despite her latest SF result. Without a FerriScan to confirm her LIC, phlebotomy treatment may have continued unnecessarily for this case.

### First FerriScan taken 2010

<table>
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<tr>
<th>Average Liver Iron Concentration</th>
<th>18.6 mg/g dry tissue (NR: 0.17-1.8)</th>
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<tbody>
<tr>
<td></td>
<td>333 mmol/kg dry tissue (NR: 3-33)</td>
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Normal range (NR) is taken from Bassett et. al., Hepatology 1998; 6: 24-29.

### Second FerriScan taken 2015

<table>
<thead>
<tr>
<th>Average Liver Iron Concentration</th>
<th>1.5 mg/g dry tissue (NR: 0.17-1.8)</th>
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<tr>
<td></td>
<td>27 mmol/kg dry tissue (NR: 3-33)</td>
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Normal range (NR) is taken from Bassett et. al., Hepatology 1998; 6: 24-29.

Note: The area of the liver image used for the FerriScan analysis excludes large vascular structures and other image artefacts.

Authorised by: Service Centre Manager
Case Study 3: A 36 year old female survivor of acute myeloid leukemia (diagnosed at 14 years of age) did not receive a bone marrow transplant (BMT), but nearly 20 years after diagnosis iron overload was suspected and she was given a serum ferritin (SF) test which was 1011 microg/L. Around 6 months later she had a FerriScan and returned a liver iron concentration (LIC) of 13.7 mg Fe/g. Despite her borderline SF level, which in isolation may not have raised significant concern, the FerriScan result indicated that this case was close to approaching the very dangerous LIC level of 15 mg Fe/g and the care team was able to accordingly recommend phlebotomy for this patient.

In summary, these case studies highlight that SF measurements taken in isolation can be misleading regarding the true iron status of these cancer survivors. Without a reliable estimate of LIC from FerriScan, cancer survivors may be at risk of unrecognised or misdiagnosed iron overload, leading to incomplete or even unnecessary treatment. When FerriScan is combined with simple phlebotomy treatment, the guess work is taken out of the clinical management of de-ironing cancer survivors.