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Blood versus Bone marrow:

New technologies using peripheral blood can reduce the need for bone marrow biopsies

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Original reference paper:

A M Mohamedali, J Gaken, M Ahmed, F Malik, A E Smith, S Best, S Mian, T Gaymes, R Ireland, A G Kulasekararaj, G J Mufti, High concordance of genomic and cytogenetic aberrations between peripheral blood and bone marrow in myelodysplastic syndrome (MDS)

[Leukemia](#). 2015 Sep;29(9):1928-38.

Until now, bone marrow sampling has been the primary technique for routine follow-up checks on MDS patients after initial diagnosis. The bone marrow is the heart of the disease and reveals important clues, for example, about whether a patient is responding to therapy or whether the disease is stable or worsening (progression).

During the procedure, which can be uncomfortable, an aspiration from the patient's marrow is taken, and specific blood cells derived from the bone marrow are analysed, allowing clinicians to monitor the ongoing disease status of a patient.

More specifically, clinicians may look for the presence of particular genetic mutations within the cells, what the DNA chromosomes physically looks like (a technique broadly called cytogenetics) and the shape of certain bone marrow blood cells (morphology).

However, although necessary, bone marrow biopsies have many downsides. Most notably the stress and physical discomfort to the patient, for which some patients require sedation. It is an invasive procedure which therefore always carries a risk of infection. This risk also increases in elderly patients, or those with a low or very low neutrophil (white blood cell) count. This makes frequent sampling problematic which means patients may not be followed as closely as clinicians would like. Overall, for many patients, regular biopsies are yet another 'painful' and inconvenient aspect of living with MDS.

An easier alternative to a biopsy would be a peripheral blood (PB) sample (i.e. the blood already circulating in the body, which is produced in the bone marrow). Until recently, it had not

been conclusively shown in a large scale study that PB could be used to obtain similar results as a bone marrow biopsy. Also, the commonly used testing technique, called metaphase cytogenetics, does not work very well for PB samples. Therefore until now, there has been little momentum in adopting a PB sampling as standard practice.

However recent research by a group at Kings College London and the Hospital may change that (A M Mohamedali *et al*). Their research has demonstrated that peripheral blood samples are an equally accurate and reliable source for monitoring the genetic mutations in bone marrow derived blood cells, and hence for monitoring the disease status of a patient (please see below for full publication details).

The research group looked for the presence of various genetic abnormalities known to be frequently associated with MDS in both bone marrow samples and PB samples, and compared the results against each other.

In order to do this, they used two specific testing methods which do work for PB samples. The first is a technique called SNP – Array karyotyping (a method used to identify changes to the number of DNA strands in a cell, a feature commonly observed in MDS). The second technique used was next-generation sequencing technology (NGS) to look at over 20 genes known to harbour mutations in up to 80% of MDS patients. They found that if a gene mutation or changes to the number of DNA strands could be detected in a bone marrow biopsy sample, it could also be detected in the PB sample of the same patient. Overall, they found that the same results could be obtained for both bone marrow biopsy and PB samples using these techniques (there was a 98% concordance in results, which is extremely high).

These are very promising results which demonstrated proof of concept that PB can be used as a substitute for bone marrow biopsies. The authors of the publication recommend the use of PB for follow-up checks and believe that PB sampling has many distinct benefits over bone marrow sampling.

The most obvious being the fact that the method is less invasive and virtually pain free, with little or no risk of infection. This allows for more frequent check-ups which in turn enables closer disease monitoring for better outcomes. The procedure is also quicker and easier to perform than a biopsy, and as no sedation is required, patients are also able to leave immediately with no recovery time required.

Aside from patient benefits there are also important advantages for hospitals too. The procedure is easier and quicker to carry out than a bone marrow biopsy, therefore does not require specialist staff and cuts down on procedure time. In some cases it may even free up hospital bed time and offer cost savings.

Additionally, once the PB sample is taken, it can be analysed relatively easily using the two testing techniques described by the research group. Both the SNP – Array karyotyping and 21st century sequencing techniques were semi-automated, reliable and provided robust results, making it attractive for hospital diagnostic labs to implement.

Although a bone marrow biopsy will always be essential for initial diagnosis, finding easier, less painful, yet still accurate and reliable ways to monitor MDS patients represents a major improvement. PB sampling could spare a large population of patients the need for repeat bone marrow biopsies, making the burden of their disease a little lighter, and allowing clinicians to follow patients more closely through more regular checks.

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Clinician/researchers/authors quotes:

“This research has provided us with the very important information that the genetic abnormalities found in the bone marrow of MDS patients are also detected in the blood. We already know that many patients acquire new genetic abnormalities during disease progression and it would therefore be possible to monitor for this on a blood sample. At present the main limiting factors for adopting this approach are the cost of these technologies as well as the complexity of analysing the data produced. The price will however fall over time and we will continue to simplify the data analysis process meaning that this has real potential for the future management of MDS patients. Unfortunately I don’t think this will replace the need for a bone marrow biopsy as this remains critical in confirming disease progression however it may allow us to detect changes early and determine when this procedure should be performed. Further research will be needed to find out if this can improve the overall management and outcome in MDS patients.”

Dr Catherine Cargo, Consultant in Clinical Haematology

Haematological Malignancy Diagnostic Service (HMDS), Leeds Teaching Hospitals NHS Trust

“From a clinical perspective, this study is the first of its kind to demonstrate the potential use of 21st century technologies in improving the management and treatment of human diseases, especially in a disease like MDS where the majority of the patients are of old age (> 70 years). This study has clearly shown that the genetic analysis that is usually performed on bone marrow biopsy can also be reliably done on peripheral blood, thus potentially eliminating the need for repeated painful and expensive bone marrow aspirations for disease monitoring. That being said, further larger studies involving multiple centres are needed to verify these results before being introduced into routine clinical practice. Although there are challenges that need to be addressed including the cost and the data management as well as interpretation of the results, however, this technological advancement has great potential for the clinical management of MDS patients and will also help in early intervention where disease progression is suspected.”

Syed Mian, PhD, Research Associate (one of the authors of this research paper)

Department of Haemato-Oncology, King’s College London

“Currently only a handful of specialist laboratories are equipped to perform SNP-Array karyotyping or next generation sequencing mutation analysis in MDS. The number of centres tends to be small because these types of analysis are highly specialised, require the use of expensive, dedicated equipment and require highly skilled and experienced staff. These laboratories tend to be within specialised Haematological Malignancy Diagnostic Centers such as the service in Leeds Teaching Hospitals NHS Trust and my laboratory within King’s College Hospital London. The cost of these investigations is relatively high, however the amount of genetic information obtained using these methods is much greater and results in improved certainty of diagnosis. Some of these genetic findings are also useful for informing clinicians and patients about the likely course of the disease and can also influence treatment options in a way that the conventional methods may not. Here at King’s College Hospital we have been performing this next generation sequencing mutation analysis and SNP-array karyotyping in MDS for several years. We have performed analysis on hundreds of samples and these analyses are now available as diagnostic tests. Access to these analyses make replacement of some bone marrow biopsy samples with blood a reality for our patients.”

Nicholas Lea, PhD, Clinical Scientist

Laboratory for Molecular Haemato-Oncology,

Department of Haematology, King’s College Hospital London

“Our study was designed primarily with the patient benefit in mind. Being a tertiary referral centre for MDS, there was a clear need to improve on existing methods in aiding patient diagnosis and enable frequent follow up of patients. The data is an extension of our earlier publication in the journal Blood (2013) and confirms the very high concordance of the genetic information obtained from the bone marrow and peripheral blood. I am delighted that MDS UK has taken the initiative to disseminate this information to the community so that patients may benefit from cutting edge research tools to help and with their MDS journey”

Dr Azim M Mohamedali, PhD Senior Research Fellow

Department of Haemato-Oncology, King’s College London

MDS UK – Note to patients

If you are not yet offered the choice of peripheral blood (PB) sampling during routine check-ups and would like more information about its use, please contact MDS UK. This is a fairly recent technology, therefore if your haematologist has not yet started using it please hand a copy of this article to him/her. We would be happy to provide more information directly to you and/or your haematology consultant.

MDS UK – Note to haematologists

Further details about this technology can be found via:

Research paper in [Leukemia](#). 2015 Sep;29(9):1928-38. doi: 10.1038/leu.2015.110. Epub 2015 May 6

MDS expert group website: <http://www.ukmdsforum.org/>