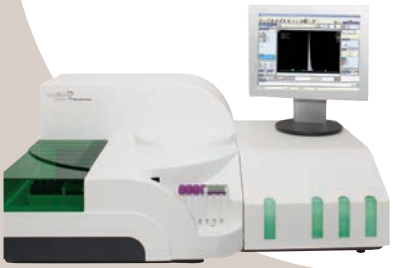
Sebia Focus - N°9

October 2013

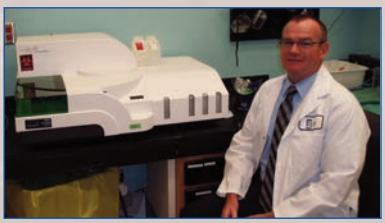


Implementation of HbA1c on CAPILLARYS 2 Flex Piercing in the Molecular Hematology Laboratory at the McMaster University Medical Centre (MUMC), Hamilton, Ontario (Canada)

Andrew Mc Farlane has worked for many years in Transfusion Medicine, Special Hematology and Molecular Diagnostics. He received his Advanced Registered Technologist (ART) in Hematology in 1993. In 2000, Andrew Mc Farlane became the senior technologist in the Hemoglobinopathy laboratory at St. Joseph's Hospital, Hamilton, Ontario. In 2003, he advanced to the position of Technical Specialist, Molecular Hematology and Red Cell Disorders, and is currently Supervisor of Genetic services at HRLMP. Andrew Mc Farlane received the Distinguished Fellowship from CSMLS in 2010 (FCSMLS) and completed a Masters of Science (MSc) in Clinical Research Administration (CRA) in 2012. He holds a part-time faculty appointment with the Department of Medicine, McMaster University, Hamilton, Ontario being involved in teaching of medical residents and Fellows.

Andrew Mc Farlane is a national and internationally respected expert in the area of Molecular Hematology, hemoglobinopathies and red cell disorders, has recently published a book chapter, several peer-reviewed journal articles, numerous scientific abstracts and been an invited guest speaker at several international conferences.

Can you briefly describe the Molecular Hematology Lab at MUMC?



Andrew McFarlane
Molecular Hematology Lab

The Hamilton Regional Laboratory Medicine Program, (HRLMP) in Hamilton Ontario Canada is formed from 2 hospital corporations that services 3 hospitals, 2 urgent care centres, a regional cancer center and a regional laboratory reference centre for sample referrals from other healthcare institutions and laboratories. We employ a staff of approximately 700 people, providing laboratory services for 1900 inpatient beds for about 2.2 millions people in Hamilton and surrounding regions.

The Molecular Hematology laboratory is at the McMaster University Medical Centre (MUMC) site. This is a laboratory within the HRLMP that specializes in the Red Cell Disorders providing Hemoglobinoapthy screening and has been designated as the Provincial Hemoglobinopathy DNA Laboratory for confirming variant hemoglobins or thalassemia by molecular analysis. We also do molecular confirmatory testing of Newborn Screening Ontario positive samples for sickle cell screening as well as referrals from other health care centres and laboratories centres across Canada.

You have been using CAPILLARYS technology for a long time in your laboratory for the initial screening of hemoglobin disorders. We can even say you are a pioneer in this field. Recently, decision was made to transfer the HbA1c testing from the Clinical Chemistry and Immunology Lab (Hamilton General) to the Molecular Hematology Lab at MUMC. Why this decision?

The Red Cell Disorders laboratory has been using the Sebia CAPILLARYS since 2006 for routine primary hemoglobinopathy screening. We upgraded to the CAPILLARYS 2 Flex Piercing in 2011. We then decided to evaluate this system for HbA1c when it became available in Canada late 2011.

There was ongoing discussions with our special chemistry group at HRLMP for developing a plan to perform a comprehensive evaluation and comparison with our current HbA1c analysis and point of care (POCT) systems. These discussions with the chemists were initiated early in 2012 and a plan for the evaluation was agreed upon by mid 2012. The evaluation was done in November and results were accepted so we made the transition to the Sebia CAPILLARYS 2 Flex Piercing HbA1c in March 2013.

How did you evaluate the SEBIA CAPILLARYS 2 Flex Piercing HbA1c method?

After investigating the possibility of the CAPILLARYS 2 Flex Piercing for HbA1c testing, we learned it had the potential for:

- Higher throughput, up to 37 tests per hour
- Very low CV's – stated to be 2% or less
- Using calibrators which are IFCC traceable

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- Using the same calculation formula used by the IFCC reference method for the worldwide assay standardization: HbA1c/(HbA1c+HbA0).
- Having no interference with labile HbA1c
- Having no interference with the major Hb variants- S, C, E and D
- Having limited interference from HbF = Up to 15% HbF

The project involved a joint effort for planning between our special chemistry, hematology, POCT team and quality manager. There was good communication to define the evaluation model including analysing the workflow, equipment installation qualifications, equipment operations qualification and performance qualification.

We wanted to ensure we could maintain a high quality and level of service for reporting the HbA1c so we looked at the following parameters during the evaluation:

- Comparability to current methodology and POCT
- Precision
- Measure interference of HbF
- Check for carry over
- Linearity
- Interference from Hb variants
- Workflow (sample prep, analysis, throughput, reporting etc)

What analytical performances were highlighted during your evaluation of the technique?

The CV values we found for both inter-run and intra-run precision using patient samples and control samples were acceptable within 2 % stated by manufacturer. Accuracy testing compared to our present system found a slight positive bias of 0.4% on the Sebia CAPILLARYS 2 Flex Piercing. However, we considered this bias to be attributable to our routine method since no significant bias was found when comparing the Sebia CAPILLARYS 2 Flex Piercing system with an alternative HPLC method. The linearity was also acceptable within concentrations tested, ranging from 4.7 to 16.4 % and when repeating linearity analysis the CV values were less than the manufacturer's expected 2 %. Carryover studies showed no detectable carryover between samples across all capillaries and our studies demonstrated no significant interference from Hemoglobin F levels up to 15% or from 33 different variant hemoglobins tested.

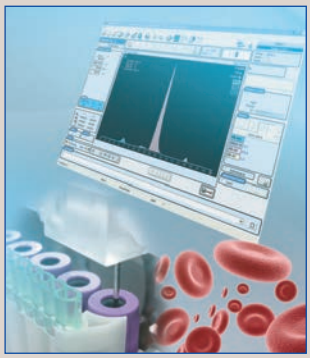
And what about the ergonomics of the system?

The CAPILLARYS 2 Flex Piercing system was good for reducing some of the preanalytical preparation for our samples. We were able to just load the system and go. We developed a workflow that included a Medical Laboratory Technologist to set up the CAPILLARYS 2 Flex Piercing in the morning and run controls at the beginning of the run then utilized one of our Medical Laboratory Assistants (MLA) to continuously load the system during the afternoon. The results would then be reviewed by the technologist and released to our laboratory information system (LIS). Moving forward we are investigating the possibility of implementing auto-verification of these results which should improve workflow efficiency.

How does the HbA1c assay complement the Hemoglobin assay on CAPILLARYS 2 Flex Piercing?

The CAPILLARYS system works well with our hemoglobinopathy screening using the same system. The switch over to running the hemoglobin assay is fairly simple. We are able to batch our hemoglobin assays and run once or twice per week. It can easily be done within one day. Using the same system for our hemoglobinopathy analysis is great because any samples that have a variant are stored in its database so when we get a repeat sample from the same patient, the previous results are linked and we know these patients have previously been identified as having a variant. The previous HbA1c results are also available in the database so we can see trends in patients helping to alert us when they may be going out of control.

What is, in your opinion, the strongest added medical value of this new technology?



There are many good features that are advantageous in this new technology but I think the most useful for our lab is the ability to detect the hemoglobin variants and to determine if these variants might interfere and lead to erroneous HbA1c values. Related to this is the linking of the HbA1c analysis with the hemoglobin assay in the systems database, which is a huge advantage for our lab.

One of the unique feature of CAPILLARYS 2 Flex Piercing HbA1c is its ability to separate and quantify HbA2 from the HbA1c profile, allowing the incidental discovery of beta-thalassemia during diabetes diagnosis[1] or follow up. Do you see any benefits related to this feature?

Yes, definitely, the detection of a possible elevated HbA2 in our situation has a huge advantage because we can suggest follow up testing in these patients. Our laboratory has developed some standard comments to report a possible beta thalassemia to the patient's doctors. If we get the elevated HbA2 value using the HbA1c assay we report a "canned text comment" to alert the doctor that their patient may have a thalassemia and if they are not already aware of this fact a hemoglobinopathy screen should be done. We have also identified several patients that have hemoglobin variants including a few patients that had previously undiagnosed sickle cell disease. We report a similar comment to alert the clinicians ordering the HbA1c. This is a huge improvement for patient care and could potentially prevent unnecessary medical interventions or clinical consequences due to these thalassemia and clinically relevant hemglobinopathies.

You have communicated a Memorandum* to your clinicians in order to explain the reasons for this change in methodology and location for HbA1c testing. How did your clinicians react to this change?

Overall the clinicians were pleased with our changes. We improved our reporting format for identification variant hemoglobin with ability to confidently report the HbA1c value in the presence of common hemoglobin variants as well as identify patient with a possible beta thalassemia. As far as I am aware we have not received any negative feedback from our clients. In fact we have received requests through our Laboratory Reference Center for some external laboratories that would like to use our service to perform their HbA1c assays because of this improved service. We originally were expecting to perform an average of 80 to 100 samples per day and within the first three months the numbers have averaged 120 per day with increased interest from external clients from outside our hospital system. I think this speaks to the improved service with switching to the new technology.

**http://www.hhsc.ca/workfiles/HRLMP/LRC_COMM/HbA1c%20-%20Change%20in%20Methodology%20and%20Location%20-%20February%2015,%202013.PDF*

[1] Note: the HbA1c test is not authorized in some countries for the diagnosis of diabetes.

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