Oligoclonal Banding Patterns in Patients with Multiple Sclerosis

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Background

Multiple sclerosis is one of the most common neurological diseases in Canada among young adults and frequently leads to disability. Current understanding of the disease suggests that autoimmune mechanisms play a pivotal role in development and progression of the disease. While it is well established that T-cells induce a cellular response leading to demyelination and axonal loss, the role of antibody producing B-cells is becoming increasingly more apparent [1].

Oligoclonal banding (OCB) detection in the cerebrospinal fluid (CSF) has been used clinically as an indicator of Multiple Sclerosis (MS) for many years. About 95% of patients with clinically definite MS show oligoclonal IgG antibodies in their CSF [2-4]. Although the antigens responsible for the autoimmune response are not well established, it has been shown that the absence of detectable bands is associated with a "milder" course of the disease while patients with IgM bands specific to myelin lipids have a more aggressive course of disease [5-6]. In addition to this, Lin et al has recently analyzed the specific banding patterns of patients with positive OCB in detail and found two distinct patterns which they have named theta and delta. The delta pattern had multiple prominent bands which were discreet and well-defined, while the theta pattern had fewer and fainter bands [7.]. In their study, the theta pattern had no association with MS despite being positive for OCB [7]. These studies highlight the need for further research into the banding patterns found in CSF analysis.

Objectives

1. To confirm findings of theta and delta subgroup banding patterns and their association with a clinically definite diagnosis of MS.

2. To investigate if there are subgroups of OCB patterns based on **band migration distances** among patients with a clinically definite diagnosis of MS

Methods

Delta and Theta Banding Confirmation

A descriptive study using retrospective data from Jan 2012-Dec 2014 was performed. All positive OCB tests from the Fraser Health region during this time period was assessed for delta and theta banding. Patient data and diagnosis of MS was then retrieved from electronic hospital records. Patients with uncertain or pending diagnosis were not included in the final analysis.
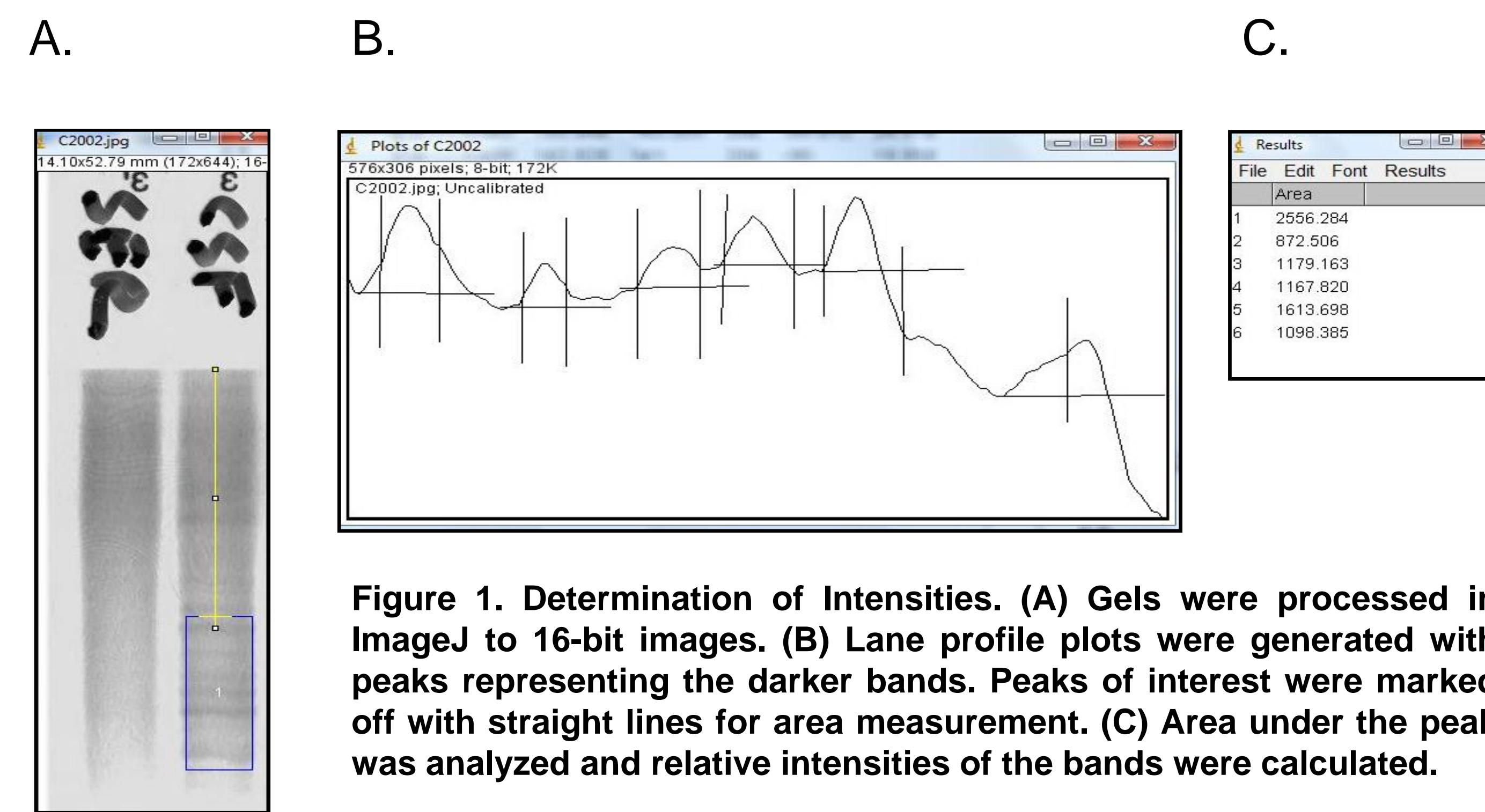
Subgroup Investigation

The OCB gels from the patients with delta positive banding and a clinically definite diagnosis of MS were scanned and evaluated in the image processing program, ImageJ *. Theta pattern, weak banding, CIS** patients, and gels with staining from age were not included due to the limitations of the imaging program. The relative band intensities were determined and the migration distance of the three most intense bands in each sample were recorded (Figure 1)

*ImageJ is an image processing and analysis in java program available through the National Institute of Health available publicly here: http://imagej.nih.gov/ij/index.html

**CIS= Clinically Isolated Syndrome

Determination of Intensities

A.   B.   C.

Figure 1. Determination of Intensities. (A) Gels were processed in ImageJ to 16-bit images. (B) Lane profile plots were generated with peaks representing the darker bands. Peaks of interest were marked off with straight lines for area measurement. (C) Area under the peak was analyzed and relative intensities of the bands were calculated.

Theta and Delta Banding Patterns

A.

Year	Total Positive	Omitted	Total Samples Used	Theta	Delta
2014	35	11	24	6	18
2013	31	8	23	5	18
2012	28	10	18	0	18
Total	94	29	65	11 (17%)	54 (83%)

B.

	Theta		Delta	
MS/CIS	2	18%	43	80%
Other Diagnoses	9	82%	11	20%

Figure 2. (A) Percentage of theta and delta banding pattern in positive oligoclonal banding tests in Fraser Health from 2012-2014. (B) Percentages of MS patients with theta and delta banding pattern.
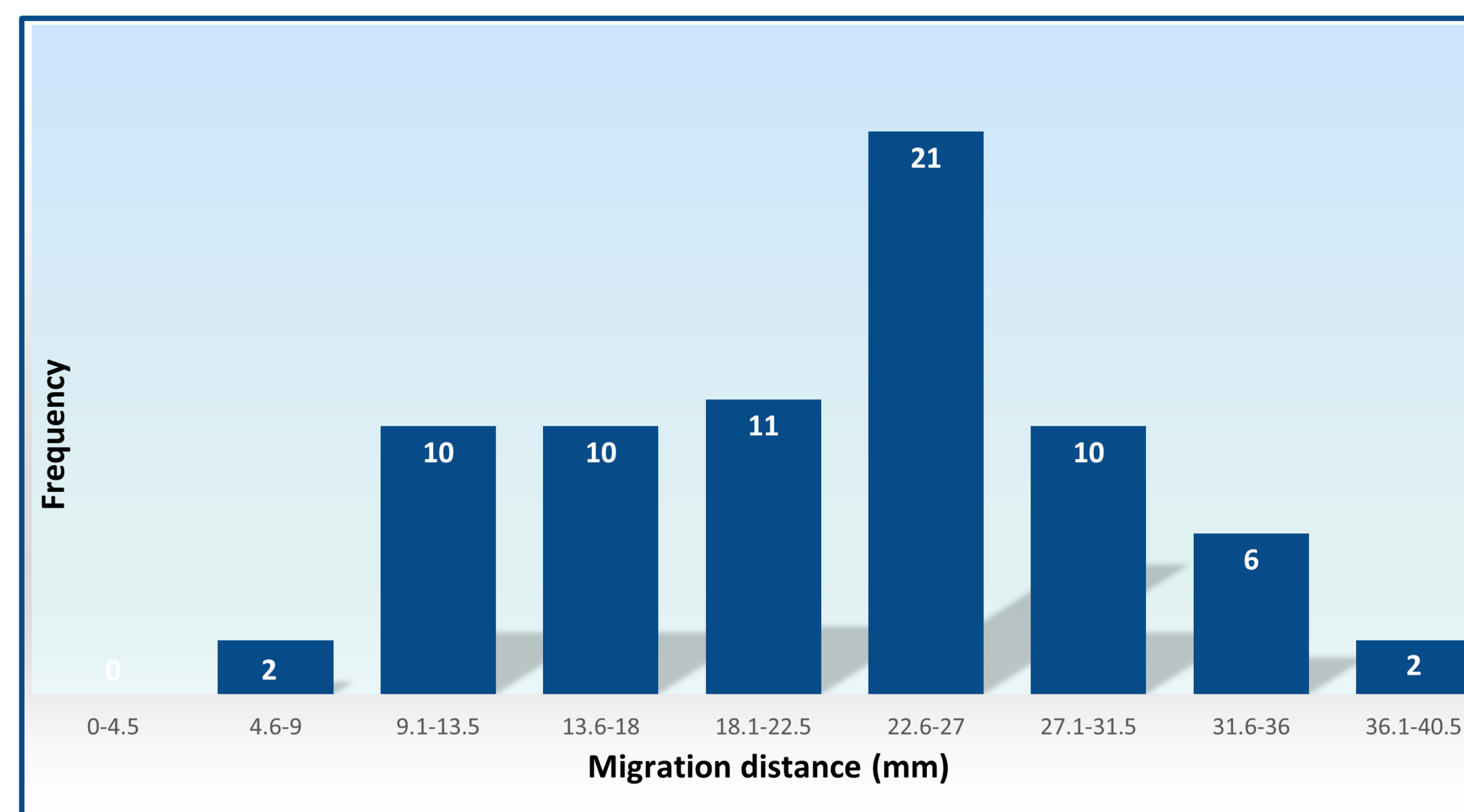

Figure 3. Frequency chart of band migration distances from MS patients with positive OCB with the delta pattern.

Results

A total of 94 positive oligoclonal banding results were identified at Royal Columbian Hospital which completes OCB testing for the entire Fraser Health Region. Of those, 29 samples had to be omitted due to uncertain or pending diagnosis, leaving 65 positive samples that were included in this study. There was some variation in the three years with 2012 having no theta samples. Overall, we found a total of 11 (17%) samples with theta pattern and 54 (83%) with delta pattern (Figure 2A). These values are comparable to the prevalence found by Lin et al. [7].

Of the delta samples, the final diagnosis was MS/CIS in 43 (80%) of patients (Figure 2B). All MS subtypes were represented. Surprisingly, there were 2 (18%) patients with diagnosed MS that were of the theta subtype. This is in conflict with Lin et al. as they did not find any patients with the theta pattern that had a diagnosis of MS. However, one of the two patients have a milder form of the disease with "very low disease activity". Of note, one of the theta patients in the "other diagnoses" category had radiologically isolated syndrome which has the potential to progress to CIS and then MS.

Analysis of the migration distance of the three most intense bands revealed a greater frequency of bands that migrated between the 22.6-27 mm range (Figure 3).

Summary

- Frequency of the delta and theta pattern in the Fraser Health Region are similar to those found by Lin et al.
- The proportion of MS patients with the delta pattern on OCB was also similar to Lin et al.
- Contradictory to Lin et al., MS patients with theta pattern were present. This challenges their conclusion that diagnostic significance can be improved by excluding theta pattern in OCB testing.
- 1/2 of the MS patients with theta pattern had a clinically milder course of disease. This could suggest a possible subgroup of MS patients.
- Increased migration of bands to 22.6-27 mm suggests a possible subgroup of MS patients. Further investigation and clinical correlation is needed.

Acknowledgements

References

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