# LITHOS

## The Memorial University Medical Journal

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# LITHOS

## *The Memorial University Medical Journal*

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## Editorial Board



Cover photo courtesy of Dr. Hasan Al-Obaidi, MD


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# Land Acknowledgement

A land acknowledgement is offered to recognize Indigenous peoples' enduring connection to their traditional territories, to recognize the history of the land that is currently shared by many peoples, and to recognize stewardship as a shared commitment of all those who reside in a territory. The practice of territory acknowledgement is itself a replication of an Indigenous practice which predates European contact.

## St. John's Campus

We respectfully acknowledge the territory in which we gather as the ancestral homelands of the Beothuk, and the island of Newfoundland as the ancestral homelands of the Mi'kmaq and Beothuk. We would also like to recognize the Inuit of Nunatsiavut and NunatuKavut and the Innu of Nitassinan, and their ancestors, as the original people of Labrador. We strive for respectful relationships with all the peoples of this province as we search for collective healing and true reconciliation and honour this beautiful land together.

# Editorial

## The significance of student-operated medical journals

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Peer-reviewed medical journals are essential to the dissemination of literature upon which the current and future understanding of medical practice is founded. These journals present an important, established, credible means of communicating the findings of clinical trials and other relevant scientific information with the medical community.[1,2] Pertaining to medical schools, there is an emphasis placed on learners in today's curriculum which promotes the development of competencies required not only of skilled clinicians, but that of clinician researchers and health scientists as well.[3,4] As such, the role of research within medical school curricula has been receiving greater attention with increasing expectations of students in regard to these academic endeavours. As an extension of the expanding role of research in undergraduate medical curriculums, there has been a global increase in the presence of student-run medical journals as a component of medical schools over the past thirty years.[5]

In Canada, student medical journals present with diverse scopes, structures and policies while operating in a dynamic setting that facilitates rapid staff turnover. However, these journals constitute an important training and mentoring opportunity for students not provided in other extracurricular activities.[6] Recently, Al-Busaidi et al. (2019) noted that in addition to playing a critical role in promoting academic research and publishing amongst medical students, publication in medical student journals was also a positive predictor of short- and long-term academic success.[7] Further, The Royal College of Physicians and Surgeons of Canada devised the CanMEDS framework which outlines the competencies required of physicians in effectively meeting the healthcare needs of the populations they serve. The core tenets of this framework include seven broad areas of professional, communicator, collaborator, leader, health advocate and scholar which integrate into the overall medical expert role.[8] It has been posited that medical student journals play an important role in building the capacity required of students in meeting the standards of the scholar, communicator and medical expert roles through the provision of training in academic writing and editing.[6] The presence of a medical journal provides an invaluable opportunity for medical trainees to gain first-hand experience in the research review process while being held accountable for research findings and study recommendations.

There are currently eleven Canadian medical schools with their own student-run medical or health sciences journals, with the University of Manitoba and Memorial University having composed their inaugural issue within the past five years. An overview of Canadian medical school journals can be seen in Table 1.

**Table 1.** Summary of Canadian Medical School Journals by Years in Operation (Adapted from Verma et al., 2011)[6]

| School | Years in Operation (as of 2024) | Journal Discipline | Average Number of Issues/Year |
|---|---|---|---|
| University of Toronto | 99 | Medical Journal | 3 |
| Western University | 92 | Medical Journal | 3 |
| Dalhousie University | 65 | Medical Journal | 2 |
| McGill University | 28 | Medical Journal | 2 |
| Queen's University | 25 | Health Science Journal | 2 |
| University of British Columbia | 21 | Medical Journal | 2 |
| University of Alberta | 18 | Health Science Journal | 2 |
| McMaster University | 18 | Medical Journal | 1 |
| University of Ottawa | 12 | Medical Journal | 2 |
| University of Manitoba | 5 | Medical Journal | 2 |
| Memorial University | 2 | Medical Journal | 2 |

The presence of student-run medical journals at several institutions across Canada has served as an outlet for students to foster creativity and develop original ideas individually or in collaboration with peers and supervisors. These established journals have shown significant benefit for medical student development as well as medical research and practice as evidenced by their purpose and longstanding histories. Additionally, Levine et al. (2019)[9] found that collaboration between medical and biomedical graduate students in these initiatives fostered a collaborative environment, as well as development of respect for each other's professions. These efforts may also allow for continued collaboration in professional settings important to the advancement of medical research and practice.

While most Canadian medical graduates successfully match to residency programs, the ability of students in the prior three graduating classes to participate in visiting electives was hindered by the COVID19 pandemic. This lack of opportunity, while an unfortunate yet necessary decision by The Association of Faculties of Medicine of Canada, limited the opportunity for medical students in the Canadian Residency Matching Services (CaRMS) match for disciplines not offered through their institution. Contributing to this challenging match process is the increasing level of competition to secure a residency position resulting from fewer positions available per applicant over time, and a lack of clear selection committee expectations.[10,11] Building on this point, previously published projections indicated that the number of current year unmatched Canadian medical graduates, along with those entering the match after failing to secure a position in previous years, will be greater than 100 individuals in the next iteration of the process.[12] The opportunity to publish in and participate on a faculty-endorsed editorial board serves to increase the competitiveness of undergraduate medical students in their CaRMS applications. Results from Lakoff (2020)[11] found that the number of research activities undergraduate medical students were involved in was significantly associated with the odds of being matched to a first-choice iteration.

Evidently, student-led medical journals have the potential to play a significant role in fostering interdisciplinary creativity and collaboration, while simultaneously providing a boost to editorial board members competitiveness in matching to preferred residency destinations.

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# Original Research: Biomedical Sciences

## Sirtuin 3 expression in the context of Relapsing Remitting Multiple Sclerosis

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### ABSTRACT

Multiple sclerosis (MS) is a debilitating disease that attacks the myelin sheath surrounding neurons in the central nervous system resulting in focal demyelinated lesions. This process is immune-mediated in nature and is thought to arise following inflammatory and metabolic alterations leading to loss of the myelin sheath. Following this, axons in the afflicted areas may recover and remyelinate or undergo axonal loss leading to eventual neurodegeneration. Current knowledge of the mechanisms involved in lesion formation and neuronal outcomes is limited. A relatively recently identified family of proteins, the sirtuins, have been found to be strongly implicated in inflammation and aging throughout the body. While some work has identified alterations in sirtuins 1 and 2 within animal models and MS samples, no such investigations have examined the related sirtuin 3 (SiRT3) protein. In our current study, we examined SiRT3 expression in MS lesions from post-mortem tissue as well as mRNA levels within CD14+ cells isolated from MS patients and controls. We found reduced SiRT3 expression within MS lesions and trends towards reduced SiRT3 mRNA levels in females as well as MS patients. Overall, our work supports the hypothesis that SiRT3 plays a role in MS, however, further studies are needed to identify the CNS distribution of SiRT3 in MS patients, how SiRT3 alterations impact CD14+ cells in MS, and whether SiRT3 may play a role in the sex differences observed in MS.

**Significance:** It is clear that both inflammatory and metabolic processes can play a role in the pathogenesis of MS, however, this requires further investigation. Sirtuin 3 is an NAD+ dependant deacetylase that plays a role in both in metabolism and inflammation and has been implicated in a variety of disease states. Herein, we present the first evidence demonstrating that sirtuin 3 may be involved or at least altered in the context of MS pathology.

### INTRODUCTION

Multiple sclerosis (MS) is an immune-mediated disorder which attacks the central nervous system (CNS) and presents with hallmark focal demyelinated plaques. The incidence prevalence of MS continues to increase and worldwide 2.8 million people suffer from the disease.[1] MS is a highly heterogeneous disease and is believed to arise through an interplay between genetic vulnerabilities and environmental factors, however, no definite etiology has yet been confirmed.[2] Most patients are diagnosed between the ages of 15 and 40 and the prevalence is approximately 3 times greater in females compared to males.[3] Early symptoms of the disease manifest as temporary neurological phenomena, such as the loss of sensation, tremors, difficulty speaking, or paralysis.[2] Most patients have slowly worsening attacks which lead to progressive and irreversible neurological and cognitive symptoms over time in a disease category known as Relapsing Remitting Multiple Sclerosis (RRMS).[2,4] While the mechanistic underpinnings that give rise to MS are not currently known, the symptoms are the result of demyelinating lesions and subsequent neuronal loss.[2] These lesions are partially the result of the infiltration of immune cells into the CNS and can be examined histologically post-mortem.[5]

To date, no treatment has reliably altered the long-term outcomes of MS, however, numerous disease-modifying therapies (DMTs) have been identified with the ability to treat symptoms, reduce relapses and slow the course of the disease.[6–8] DMTs can reduce the frequency of relapses and have been demonstrated to slow disease progression in RRMS. Due to the heterogeneous nature of MS and toxicity associated with many MS treatments each patient must be managed at an individual level.[7,9]

Biologically speaking, MS is characterized by focal lesions within the CNS classically occurring in the optic nerve, cerebellum, brainstem, subpial spinal cord, and periventricular white matter.[5] During the progression of a lesion, a large influx of inflammatory macrophages and T-cells results in a hypercellular demyelinated region. During and following myelin loss, axons stripped of their conductive sheath can either atrophy or can remyelinate from surviving oligodendrocytes and/or

newly recruited oligodendrocyte progenitor cells.[5] Over time the lesion sites become hypocellular and inactive sites can be readily identified through a paucity of Luxol fast blood staining.[10]

Microglia are the resident immune cell of the CNS and part of the innate immune system.[11] In a healthy state, microglia possess a ramified morphology and extend long projections that actively survey the microenvironment for markers of cell injury, death or infection (i.e. danger signals).[12,13] Upon contact with these signals, the projections retract and the microglia migrate to the site and begin to produce cytokines and phagocytize debris, damaged cells or pathogens.[14] Concurrently, microglia are able to modulate astrocytes to alter blood brain barrier permeability and recruit circulating peripheral immune cells.[15]

Emerging evidence has implicated microglia as having a significant biological role in the function and dysfunction of neurons. Microglia engage in bilateral communication with neurons through a variety of molecules and receptors including the CX3CL, C1q, BDNF, IL-1B, and TNF-α.[16] Interestingly, in MS specifically, 48 of the 81 genes implicated in MS are highly expressed in the microglia.[17] Furthermore, recent advances in transcriptional profiling have identified differences in microglial protein expression in healthy appearing CNS tissue of MS patients to healthy controls.[18] Additional studies have confirmed these results and found alterations between microglia found in normal appearing grey and white matter of MS patients.[19] One family of proteins that has been found to modulate microglial activation are the sirtuins.[20]

The sirtuin (SiRT) family of proteins are nicotinamide adenine dinucleotide (NAD) linked deacetylases and are highly conserved across mammalian species.[21] Sirtuin activity is linked to intracellular NAD concentration, thus the regulation of sirtuin function is partially mediated by dietary intake and fasting. Sirtuin family members are set apart by cellular localization and downstream targets. Sirtuins 3,4,5 are found mainly localized to the mitochondria, while sirtuins 1,6,7 are in the nucleus and SiRT2 is found in the cytoplasm. Mutations within these genes have been linked to a variety of illnesses, including macular degeneration[22], obesity[23], and cancer.[24–26] Despite this, there is substantial evidence to suggest that some rare alleles have beneficial effects and indeed upregulated expression of sirtuins is protective in several disorders, including cardiovascular disease and Parkinson's disease.[27,28] Thus far, sirtuins 1,2, and 3 have been well characterized. Despite their different sub-cellular locations these three proteins have highly similar protein targets including immunoregulatory proteins FOXO3a and the p65 subunit of the NF-kB complex.[29]

Given the role of inflammatory microglia and T-cells in MS, the sirtuin family of proteins has been extensively examined in the past decade.[30] Most research has focused on sirtuin 1 and sirtuin 2, as well as several genome wide association studies reporting risk alleles in SiRTs 4 and 5.[30,31] Upregulation of SiRT1 through genetic mouse models and *in vitro* activators protects axonal density, reduces neuronal death and protects from gross symptoms in the experimental autoimmune encephalomyelitis (EAE) model of MS.[20,32,33] Experiments examining human MS patients have found that SiRT1 levels are decreased in glatiramer acetate (a commonly prescribed DMT) non-responders and these levels drop in the plasma of MS patients during relapses.[34]

The story with SiRT2 is largely similar although less well-characterized. SiRT3 has been found to be downregulated in a host of inflammatory models involving CNS tissue over the past decade.[35–37] With regards to MS specifically, one preliminary paper by Rice *et al.* reported reduced SiRT3 immunohistochemical labelling in the brains of MS patients, however, they did not examine plaques specifically, identify potential cell types of interest, or present statistical data to back up their assertation.[38] While SiRT3 acts on many of the same targets as SiRT1 and SiRT2, its physiologic location inside the mitochondria means that it plays a more specific role in mitochondrial dysfunction and internal oxidative stress than other sirtuins.[39,40]

Further research into SiRT3 could possibly help explain the loss of some neurons relative to others in MS and may be a potential therapeutic target with fewer off-target effects than existing treatments. In macrophages, increased SiRT3 levels leads to reduced ROS generation while overexpression acts to increase antioxidant production through the FOXO3a pathway both in tissue culture and rodent models.[41] SiRT3 has also been implicated in the fractalkine signalling pathway, whereby increased SiRT3 levels enhances CX3CR1 expression and microglial motility while reducing inflammatory status.[42–44] In this current investigation, we sought to determine whether SiRT3 expression differed within MS lesions and whether myeloid-derived cells within peripheral blood (CD14+) reflected similar changes.

## METHODS

### *Samples*

All experiments involving human participation were approved by the Newfoundland Health Research Ethics Board. MS patients were recruited through the Health Research Innovation Team in Multiple Sclerosis (HITMS) at Memorial University of Newfoundland, St. John's, NL, Canada. Sample selection was conducted based on a pilot study (data not shown) raising the question of sex effects. All male RRMS samples present in the HITMS study were selected with the following criteria: 1. Diagnosis of RRMS 2. Male sex and 3. Not on active treatment at time of collection. Female samples closest in age to the male samples were selected on the same three criteria. Control samples closest in age to each RRMS sample donated from healthy male and female volunteers were selected. Venous blood was previously drawn from relapsing–remitting MS (RRMS) patients and healthy controls with informed consent. PBMCs were isolated following ficoll-density gradient centrifugation, and CD14+ monocytes were subsequently isolated to ~95% to 98% purity using anti-CD14 magnetic beads (Miltenyi). To examine post-mortem MS tissue, CNS sections from subcortical white matter lesions and control regions in MS patients who died of complications of MS were obtained from autopsies conducted by Eastern Health between 1999 and 2019. Paraffin-embedded CNS tissue from these samples was serially sectioned and mounted on consecutive slides. Samples included in the study were selected on the basis of having known inactive MS lesions and normal adjacent tissue in the same paraffin block.

### *Antigen Retrieval*

Slides were rinsed in three changes of xylene substitute for 3 minutes each and then sequentially in 100% EtOH, 100% EtOH, 95% EtOH, 70% EtOH and distilled water for 3 minutes each to remove paraffin and rehydrate the tissue. Slides were then submerged within a Coplin jar inside of a 1L beaker of sodium citrate buffer (10mM Sodium citrate, 0.05% Tween 20, pH 6.0) and microwaved for 20 minutes before cooling to room temperature in 10mM phosphate buffered solution (PBS).

### *Immunohistochemistry*

Following antigen retrieval, sections were rinsed twice in PBS-T (10mM PBS, 0.05% Tween 20) for five minutes each and placed in blocking solution (10% normal goat serum, 1% horse serum in PBS) for 30 minutes. Slides were then incubated in blocking solution with 1:100 SiRT3 antibody (Sigma #54072). Slides were washed through three x five-minute PBS changes and incubated for one hour in blocking solution with 1:200 anti-rabbit biotinylated IgG (Vector Labs BA-1000) and washed thrice more in PBS. HRP was attached to the biotin using the Vectastain Elite ABC kit (PK-6102) following the included instructions for one hour. Slides were washed through three five-minute PBS changes and then incubated with DAB peroxidase substrate (Vector Labs SK-4100) for five minutes and rinsed three more five-minute PBS washes. Slides were then dipped in tap water for ten seconds, coated in hematoxylin QS (Vector Labs H-3404) for thirty seconds and rinsed in running tap water for ten seconds. Slides were allowed to dry for 24 hours and then dehydrated and cover slipped with Permount (Fisher Scientific SP15100).

### *Imaging*

Slides were imaged using Cytation5 plate reader at 4X to define lesion areas and 10X to acquire images for analyses. A total of 4 areas within each lesion and immediately adjacent (4-600ums from the border) were imaged along with serial sections stained with Luxol Fast Blue and H&E for anatomical comparison. A no primary control was completed (data not shown) and no non-specific labelling was detected.

### *RNA Isolation and qPCR*

Cells were lysed in QiaZOL reagent (Qiagen 79306) and stored at –80°C. Total RNA was isolated by RNeasy column extraction with a DNase treatment step (Qiagen, 74004). RNA was quantified using a Nanodrop. For gene expression assays, RNA (200 ng) was reverse transcribed using M-MLV reverse transcriptase (Invitrogen, 28025013). SiRT3 expression assays were performed using SiRT3 TaqMan probes (Thermofisher Scientific, 4331182) and normalized to the endogenous control gene GAPDH.

### *Analyses*

Images were analysed using FIJI to extract determine the number of nuclei, SiRT3 positive cells and relative staining intensity of the non-nuclei areas of the tissue. The average between the four regions was taken and used for analysis. RNA expression fold changes were calculated using the ΔΔCt method using GAPDH as an endogenous control. Graphpad Prism 6 software was used to conduct paired t-tests for immunohistochemical results while a Student's t-test was used to determine overall SiRT3 RNA changes and a two-way ANOVA used to examine the interplay of sex and disease status.

## RESULTS

Using post-mortem CNS tissue, we examined SiRT3 protein expression within MS lesions and adjacent CNS tissue (Figure 1) and observed an overall mean integrated density (Figure 2A) increase indicating reduced SiRT3 expression in lesioned tissue compared to control regions ($p=0.0256$). There was no significant alteration in the average number of nuclei per field (Figure 2B, $p>0.10$) nor in the ratio of SiRT3+ nuclei to SiRT3- nuclei (Figure 2C, $p>0.10$).

Utilizing CD14+ cells isolated from the whole blood of MS patients and healthy controls, we assessed mRNA expression levels of SiRT3. No statistically significant differences were observed (Figure 3A, $p>0.10$), however, when stratifying the data based on sex, both females and MS patients trended towards reduced SiRT3 mRNA expression (Figure 3B, $p=0.0875$ and $p=0.1066$ respectively) while there was no interaction ($p>0.10$). Collected demographics are shown in Table 1. No effects of age or disease duration were observed (data not shown).

## DISCUSSION

Over the past decade, research has rapidly defined a role for the sirtuin family proteins in a variety of diseases, including cancer, heart disease, Parkinson's disease, and MS. Sirtuins 1 and 2 have both been linked to MS. Sirtuin 1 is increased in acute and chronic lesion sites and decreased in PBMCs in relapse phase[34,45] while some sirtuin 2 isoforms are decreased in MS lesions matching data from rodent EAE model comparators.[46] Despite these links, to date there has been very little literature published regarding a potential role for SiRT3 in MS. SiRT3 shares many pathways both up and down stream with other sirtuin family proteins, however, its location within the mitochondria, dysfunction of which is implicated in MS pathogenicity may contribute to metabolic and inflammatory disease pathways apart from other sirtuins.[47,48] We set out to determine whether SiRT3 may be linked to MS pathology through the exploration of cells and tissues from MS patients and healthy controls. A previous report from Rice *et al.* in 2012 asserted that SiRT3 expression was reduced in non-lesioned gray matter of MS patients compared to controls, however, no statistical analyses was presented, and no further papers have explored SiRT3.[38]

In this study, we compared SiRT3 protein expression levels in inactive MS lesions to adjacent parenchyma. Our findings in Figures 1 and 2 support the hypothesis that SiRT3 may be altered in the CNS of MS patients, specifically we found a reduction in SiRT3 within the lesion. In the brain regions examined, we found that SiRT3 was expressed in nearly every cell (Figure 2B), however, no gross expression changes between lesion and non-lesion locations appeared evident. Variability between lesions, both within and between individuals has been previously established and obtaining a larger sample set may have enabled an analysis of SiRT3 expression to be conducted based on lesion classification.[10] Based on evidence from other neurodegenerative diseases, we hypothesized that SiRT3 expression levels would be reduced during acute inflammatory processes within active lesions. Furthermore, it was anticipated that SIRT3 levels would return to baseline (or become elevated) in inactive and post-demyelinating lesions given the overall reduction of pro-inflammatory cell signalling.

Determining whether SiRT3 levels are altered in MS pathology may provide further insight into the pathology of the disease and help inform treatment responses in individual patients. The ability to predict treatment response using a biomarker readily assessed in whole blood would simplify treatment initiation and reduce the time between diagnoses and effective treatment. An important consideration in determining whether SiRT3 levels are altered is the means to determine this *in vivo* using a non-invasive approach (i.e. optimal predictive biomarker). Given the involvement of microglia (a macrophage) in MS lesions we opted to investigate levels of SiRT3 specifically in CD14+ (macrophage) cells. To this end, we extracted CD14+ cells from the whole blood of healthy controls and MS patients. Samples were matched for age and sex; all MS samples analyzed were derived from DMT-naïve individuals. No overall impact of MS status on SiRT3 mRNA levels were observed (Figure 3A), however, when stratifying the data based on sex and disease, we noted a bi-modal distribution in male patients whereby SiRT3 expression levels appeared to be either greater than the mean or less than it while female samples tended to cluster around the mean. Overall, female samples and MS samples both trended to have reduced SiRT3 expression, although no interaction was noted (Figure 3B). Previous studies examining sex differences in SiRT3 expression have been performed. For example, SiRT3 expression in cardiac myocytes decreased with age in females, but not males.[49] This is possibly due to alterations in estradiol mediated SiRT3 increases, however, few papers have investigated this.[50,51] In addition, animal studies have found that SiRT3 expression is decreased in male mice and contributes to greater ischemic kidney damage and poor metabolic responses to high fat diet.[51,52]

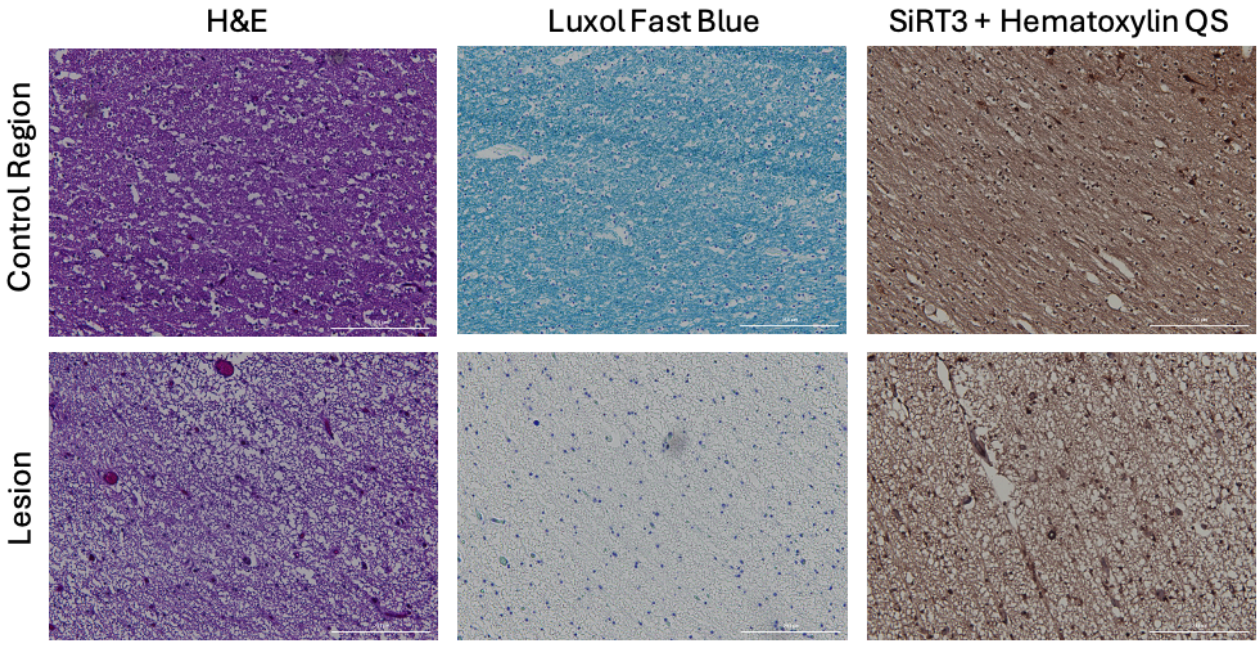


**Figure 1:** Representative images of human brain tissue (n=3) immunohistochemically stained for Sirt3 in order to identify expression patterns within and adjacent to demyelinated lesions. All lesions and control regions were located in the subcortical white matter of specimens and demonstrated reduced Luxol fast blue and H&E staining. Control sites were randomly selected adjacent to each lesion.

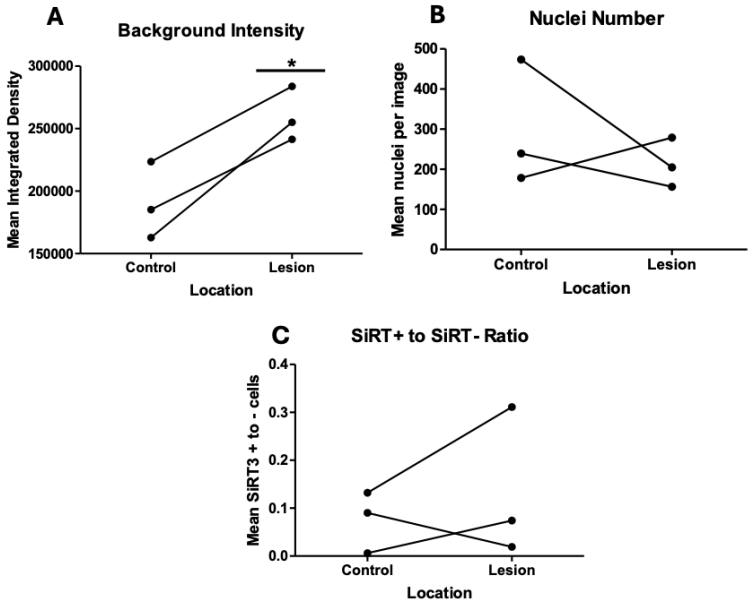


**Figure 2:** Staining in **Figure 1** was assessed by examining the integrated density of non-nuclei associated staining **(A),** through looking at total nuclei counts **(B)**, and examining the ratio of SiRT3+ cells to SiRT3- cells **(C)**. No statistically significant findings were identified in **B** or **C** using a paired t-test, however, there was an overall decrease (p=0.0256) in **A**, non-nuclei associated SiRT3 staining based on increased mean integrated density.

**Table 1:** CD14+ Cell Participant Demographics

| Group | Average Age | Average Disease Duration |
|---|---|---|
| Male RRMS n=8 | 51.8 +/- 2.2 | 13.3 +/- 3.3 |
| Female RRMS n=5 | 50.2 +/- 2.4 | 17.0 +/- 4.0 |
| Male Control n=8 | 51.6 +/- 2.9 | 0 +/- 0 |
| Female Control n=7 | 50.8 +/- 1.6 | 0 +/- 0 |

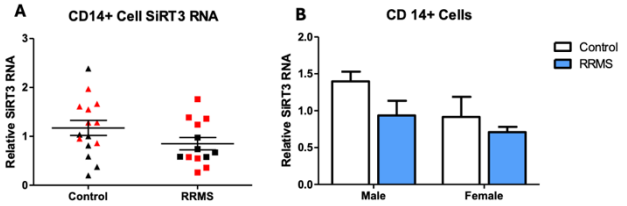


**Figure 3:** CD14+ cells isolated from peripheral blood of treatment negative MS patients and healthy controls was probed for SiRT3 RNA using Taqman primers, with means and standard error plotted. Male samples are represented in red. A) In age and sex matched samples RRMS samples appeared to have lower SiRT3 expression (p=0.12). B**)** Breaking down the population in B we found trends toward lower SiRT3 in females (p=0.08), RRMS patients (p=0.1066) but no interaction (p=0.520).

Importantly, MS is a highly heterogenous disease and a large proportion of our samples were obtained from participants who were DMT-naive and older than the typical age of first presentation. Due to these factors, it is likely that our sample represents individuals with less aggressive forms of RRMS and thus our data may not be fully reflective of the MS population. The average age of study participants could have also influenced our findings given that MS is typically diagnosed in younger individuals; the average age in our study was 51, which may also complicate identification of sex differences as some females may have been undergoing or post menopause. Further work using samples collected at first presentation with later blood draws during remission and treatment in a larger number of individuals would enable a greater level of analysis. A data set such as this could inform the timeline of any SiRT3 changes and could potentially identify whether SiRT3 levels predict treatment response or disease course. Our findings suggest that SiRT3 may be a protein of interest for further MS research and may contribute in some way to the sex differences observed in the clinical population.

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# Patient Encounters

## The search for meaning and purpose in a Uro-Oncology practice

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I met "Darryl" about 5 years ago in the spring of 2019. He had been having gross hematuria, and a CT scan had been ordered, however, he had yet to talk with anyone about the results of the CT scan.

He was called from the waiting area and I watched him stand up and walk casually into the examining room without hurry or hesitation, gesturing to a boy, about 14, as he went. The boy struck me – at 14, I expected he would return to his screen, oblivious to the world around. Not this kid – he was playing with another couple's toddler, both of them giggling. Nice kid. Grounded. Mature, despite his age.

I explained to Darryl that the blood in his pee necessitated a few investigations, and one of them was his CT scan, about which he asked me if anything had been found. I realized in a moment that I was about to tell him something terrible, and that he was completely unprepared, and that he did not have his wife with him, rather his teenage son, 14, who was patiently and obliviously waiting for him outside.

I did what I have learned to do. I looked Darryl straight in the eye. I told him I had some bad news about what the CT scan had found. I waited a beat for him to gather himself, and then he said "ok". I told him that a tumour had been found on the kidney, that it was quite large, and that he would need surgery to have it removed. His shoulders sank. He said "ok". I told him there was more … that there were also some spots in the lungs, and they were probably the spread of the cancer. Too soon to know for sure, but probably. That he would likely need more treatment at some point down the line. He asked me if the stuff in the lungs could be removed. Not safely, I told him. He asked if he was curable. I started to tell him that he probably had a few years, maybe more than that, but I only got a word or two out.

"My son." He said, "He's not … he's not ready. I need more time." He looked me in the eye, pleading, ever so slightly. A series of emotions flashed through his eyes, each of which somehow stunningly obvious to any untrained onlooker. Disbelief, fear, grief, anger, and finally: resolve. A willingness to suffer any therapy, no matter how cruel, or any procedure, whether dignity-robbing or not. For more time. For his family.

Most patients get through one or two of those emotions in a first visit like this. Or none at all. Darryl did them all in about 5 seconds. His focus on his family's need for their father's presence, for however long as could be had, was the beacon he would carry to the end.

"When can we do surgery, doc?"

"Three weeks. You'll meet with the anesthetist first. They'll make sure we're good to go. Then we'll get the kidney out. It's a big surgery given the nature of your tumour, but you're young and I think it's reasonable to assume you'll recover well, and then we probably move on to treatment over at the cancer centre."

"Is this curable?"

"With luck in the surgery, and a good response to treatment, you could get years, not months. But not a cure. I'm sorry."

"My boy. I need to see him graduate. He needs to help my wife with the youngsters. He's not ready."

"We're gonna do everything we can to keep you well for a long while. Let's get through the surgery and see where we land."

He held back a tear and asked for a few minutes with me to gather himself before facing his boy in the waiting room. I handed him a box of Kleenex. We talked logistics, a bit. Then some small talk. The Leafs. The situation settled. To a point. I put my hand on his arm, and I looked him in the eye.

"If you want to talk about this more, call my office and we'll set it up. I do a lot of these kidney cases. I will take good care of you." I shook his hand firmly. "I'll see you in a couple weeks, Darryl. We'll get the damned thing out."

Darryl sailed through the surgery. No problem. Home faster than expected. Back to work weeks before I had told him it was safe (construction, no less), but he did great. Energetic, spry, fit. No trouble at all.

The spots in his lungs didn't grow, at first. Small, but fairly convincing for metastatic disease, they just hung there, stubborn and menacing, on subsequent imaging. A year passed. All the while, Darryl told me a little about his family. Two kids younger than the teenage son, much younger. Rural Newfoundland. He was showing his oldest, the son I had seen that day in the waiting room, how to look after the house when he was gone, how to help his widow-to-be get through what would be a Hell of a task – shouldering grief, loss, loneliness and the daily grind, with three kids in tow. On a single mom's salary.

Then the spots grew. Typical Darryl, just a momentary tear, processing the implications -- domestic, financial, emotional, in a matter of seconds. All there in his eyes. Plain as day. Then determination:

"How many of these treatments are there?"

Darryl moved on to the cancer centre. They did their usual over there: stellar. He went through first, second- and third-line treatments. A few years passed. Darryl worked his job the whole way. Never complained. Just kept going. From time to time he would stop in to my clinic, give me an update, let me know what was the latest on his last and most important project: Getting the family ready for his departure. He started losing weight Spring 2023 but kept on.

The boy graduated high school that June. Darryl was there, on his feet no less, to cheer him on. But his weight was down again and the news the following month at the cancer centre wasn't good. They were out of options, and the cancer was now in liver and lymph nodes, not just the lungs. Later in the summer, it was Darryl's son who convinced him that he could take a break, and die in peace, surrounded by his family. Convinced his father that they were ready to face it. I had to close the door to my office to read the last couple lines of my colleague's note about the family. I could hear it myself: The part where the boy tells the father it's ok to let it go. I got this, Dad. I'll do my part to help Mom through.

I cannot bring myself to open Darryl's chart at this point. I know that last note from palliative care is coming, but I always want to think of Darryl alive, fighting, stoically. Nobly.

Nietzsche once wrote:

"He who has a why to live for can bear almost any how".

Darryl embodies this for me. He has lived his life in a way I hope I can emulate. When I am frustrated, worried, angry, despairing – you name it – I try to remember that my focus should be on what is best for my family. Do whatever it takes to make them ready for the time when I cannot be there (or should not be there) to protect, to provide, to nurture. This is all a father can do.

I am approaching the age Darryl was when we had our first fateful conversation. I've got an oldest boy myself. There, but for the grace of God, go I. Until such a time, I will focus on my family. Get them ready for when I might not be there. Or if I am luckier, for when I don't need to be there.

* * *

# Patient Encounters

## Beyond the surface: A medical student's perspective on esophageal dysphagia

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Silence filled the medicine floors of St. Clare's Mercy Hospital one night during my core-clerkship rotation, only to be broken by the buzz of my pager at 4 am. I jolted awake from my sleep to find a request from my senior resident asking me to see a consult in the emergency room. Eager to be helpful, I threw on my scrubs, now wrinkled from being tossed in the corner of my call room a few hours earlier and headed downstairs.

In the emergency room, I grabbed the patient's chart and began rapidly shuffling through the pages assessing her vitals, lab work and medications. I read the consult note which read "?DYSPHAGIA". At this point in my training, I had very limited exposure to the work-up of dysphagia, so I scoured my brain to remember a lecture from the previous year. I thought to myself "Remember Kevin, bird-beak sign for achalasia…" and I started creating a mental checklist for a rudimentary differential diagnosis.

I walked over to the observation area of the emergency room, where I met an older woman in her eighties who was sitting in a dimly lit patient room. Her daughter was at the bedside, and they were visibly exhausted yet relieved to see a member of the healthcare team after a long night in the emergency room. Mrs. W recounted her struggle with progressive dysphagia over the past few months and how it was negatively impacting her life. She tearfully shared that "food was getting stuck, and she was now having difficulties swallowing liquids". Mrs. W became very tearful as she shared that she lost 15 pounds during this period as she has been afraid to eat and didn't want another choking episode. I was stuck by this story, as I reflected on how a simple task like swallowing food could have such a profound impact on a person's quality of life.

After completing a history and physical, I informed the patient and her family that we will speak with gastroenterology in the morning and that she would likely complete an upper endoscopy to investigate the cause of her dysphagia. The family was optimistic as they had previously presented to care but were never formally investigated for this problem. Later that morning, the gastroenterology department confirmed she will be on the list for an upper endoscopy that day.

I was determined to get answers for Mrs. W and to work diligently to improve her quality of life. To our worst fears, the endoscopy revealed a large esophageal adenocarcinoma that was responsible for her symptoms. Given her age, the extent of disease, and other factors this was a terminal diagnosis. I was shocked to hear the news, and along with the rest of the medicine team, went out to the waiting room to provide consolation to the patient and her family.

We worked relentlessly in collaboration with other departments including thoracic surgery, gastroenterology, medical oncology, and radiation oncology to devise a comprehensive care plan and outline her options. I visited Mrs. W. every morning to provide her with the most recent updates, and she confided that even in her late eighties, she was "not ready to go" and requested aggressive management to prolong her life.

Her resilience and determination in the face of a terminal diagnosis had a meaningful impact on me. Despite facing a grim outlook, she wanted to keep fighting. I couldn't help but to reflect on how I would respond if I was in a similar situation – would I have the same courage to fight as she had? Once all the tests and investigations were complete, Mrs. W. was set to receive radiation therapy, followed by an esophageal stent and daily PPI to improve her symptoms. All of her follow-up appointments were scheduled, and Mrs. W. was hopeful that she could live out her days in dignity.

This experience underscored the transformative impact that internal medicine physicians can have on their patient's lives through a collaborative approach to care. Taking the time to have in-depth discussions with Mrs. W set the foundation of her care plan including end of life goals. It reminded me of the privilege and responsibility we hold as doctors – to treat, to comfort, and to inspire hope. As I continue my training in internal medicine, my interactions with Mrs. W. and her story of resilience will serve as a reminder of the preciousness of life and the profound impact we can have on the patients we serve.

**Note: Basic demographic information has been modified to respect for privacy and uphold patient confidentiality.**

# Case Report

## ATV Handlebar Impalement of the Upper Extremity: A Not So Humerus Case Report

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**ABSTRACT**

All-terrain vehicle (ATV) ownership in Newfoundland and Labrador, Canada has been increasing over the past two decades, likely owing in part to the province's predominantly rural geography and increasing utilisation in the tourism and recreation industries. As such, accidents while operating these recreational vehicles have become increasingly common and are frequent presentations to rural emergency departments. Our case documents a healthy 59-year-old female who sustained a significant upper extremity penetrating injury sustained while operating a recreational ATV. This case emphasizes the importance of utilization of human resources standardized management pathways in NL.

### INTRODUCTION

A steady increase in all-terrain vehicle (ATV) ownership has been observed over the past several years due in part to significant interplay within the tourism and recreation industries. Secondary to increasing utilisation, there has been a rise in the occurrence of serious ATV-related trauma, morbidity, and mortality.[1–3] ATV accidents are commonplace presentations to rural emergency departments (EDs). Approximately half of the residents of the province of Newfoundland and Labrador (NL) are considered to live rurally, residing in geographic areas with a population of fewer than 10,000 individuals.[4] As such, NL reported increased incidence of ATV-related injuries and fatalities compared to other Atlantic Canadian provinces.[2] Here, we present a unique case of a low-speed ATV rollover in rural NL, resulting in a penetrating upper extremity trauma with prolonged recovery course.

### CASE PRESENTATION

A healthy 59-year-old female presented to a rural ED via emergency medical services following a single vehicle accident while operating a recreational ATV. The patient lost control on loose gravel and careened over the oncoming trail embankment, resulting in a right-sided rollover which pinned her under the ATV. The patient was wearing a helmet and did not suffer head trauma or loss of consciousness. However, her right arm was entrapped and impaled by the handlebars of the ATV.

Arrival of the rescue team revealed the patient to be in significant pain with embedding of the handlebars into the medial portion of the right arm above, yet not traversing, the antecubital fossa and appeared to involve the distal upper extremity. Trailside extraction was performed by volunteer firefighters who utilized a hydraulic rescue tool, commonly referred to as "jaws of life," to carefully sever the ATV handlebar and clear the vehicle from her antecubital fossa. The patient described paresthesia along the ulnar nerve distribution into the right fourth and fifth digits while denying pain in her neck or additional extremities. She was boarded and cervical collar was applied while the foreign body was secured with gauze and cling to minimize movement. The patient verbalized an allergy to penicillin and was injected with ketorolac for pain relief and immediately transferred via ambulance to the nearest rural ED.

Initial assessment revealed the ATV handlebars embedded in the arm just distal to the antecubital fossa and did not traverse the axilla (Figure 1). Normal vascular and neuromotor examinations were documented, with palpable ulnar and radial pulses on serial exams. On musculoskeletal examination, flexion and extension of all digits of the right hand was preserved but the patient had weak to absent abduction. Antibiotics were not administered upon presentation to the ED.

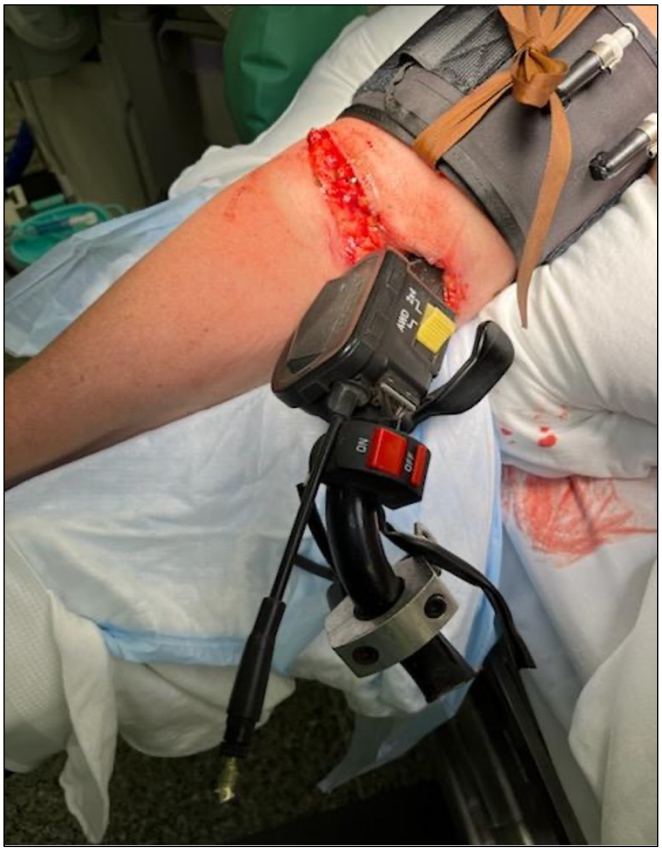

**Figure 1.** Initial assessment revealing ATV handlebars impaled into the right antecubital fossa.

Advanced trauma life support (ATLS) protocols were then implemented with immediate laboratory trauma investigations notable only for slight hypokalemia of 2.9. A complete blood count (CBC) revealed leukocytosis of 20.2 with stable hemoglobin and platelet counts of 137 and 353, respectively. Computerized Tomography (CT) of the full spine, chest, abdomen, and pelvis revealed no acute traumatic injury. Further x-rays of tibia, fibula, femur, knee, and ankle were also unremarkable. X-ray of the right humerus, elbow, and radius/ulna revealed the obvious handlebar foreign body without evidence of fractures (Figure 2). Upper extremity angiography was attempted, however, non-diagnostic due to the combination of inability to appropriately position the extremity with the CT gantry, as well as significant beam hardening artifacts from the handlebar (Figure 3).

Trauma management included morphine 10 mg IV along with dimenhydrinate 25 mg IV. Potassium chloride 40 meq IV in 1 L of Normal Saline was given over 4 hours to correct the hypokalemia. A tetanus 0.5 ml intramuscular injection and insertion of a foley catheter were completed prior to stat consult to local general rural surgeon. Following discussion with the tertiary trauma centre and plastic surgery, a plan was developed for surgical exploration and removal of the ATV handlebar foreign body to be managed locally, irrespective of presumed nerve injury.

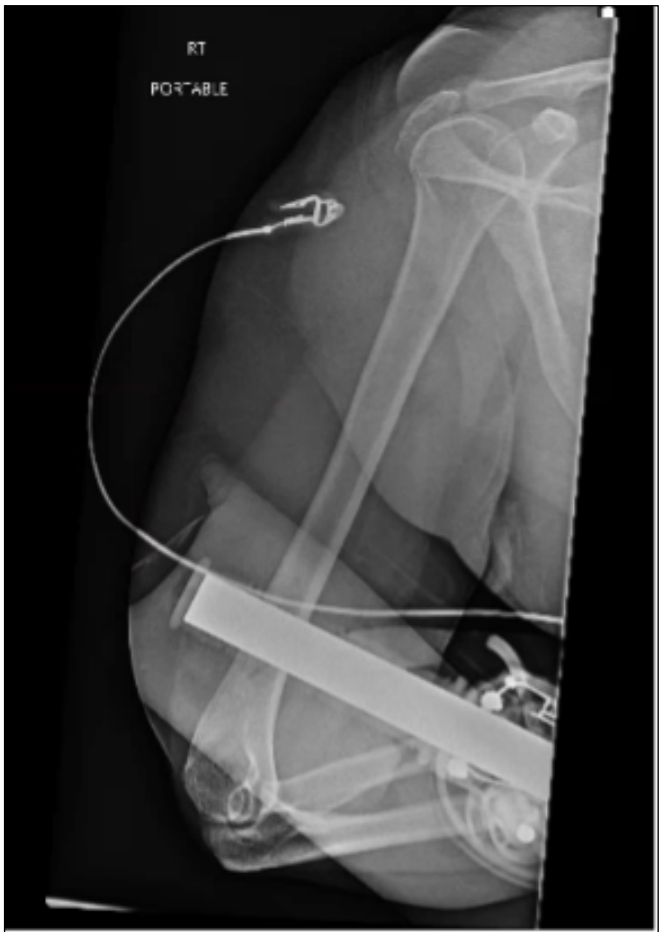


**Figure 2.** Plain film radiograph showing ATV handlebars embedded in the right upper extremity.

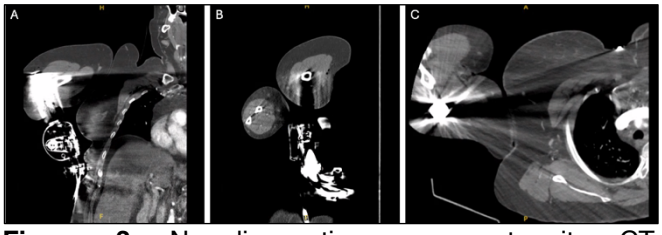


**Figure 3.** Non-diagnostic upper extremity CT angiography displaying difficulty with positioning and significant beam hardening artifacts from the handlebar. A) Coronal plane B) Sagittal plane C) Axial plane.

Patient was transferred to the operative theatre and general anesthetic administered along with intraoperative intravenous ceftriaxone. Careful examination did not reveal any obvious vascular or neurological injury as well as appropriate visualization of brachiocephalic structures. The handlebar was gently removed, and the tourniquet slowly released after which a few small bleeding vessels were cauterized, and the wound irrigated with copious amounts of sterile water. Prior to primary closure some de-vascularized tissue was excised using a combination of hot cautery and sharp dissection, after which a Penrose drain was placed (Figure 4).

Four days postoperatively, the patient was transferred to the tertiary care centre to be assessed by plastic surgery. She reported increased numbness and tingling in all digits of her right hand, and she had obvious claw deformity of the ring and little fingers. Urgent MRI of the right elbow was ordered to determine the extent of ulnar laceration and appropriately prognosticate the present case. Results of the MRI revealed absence of direct transection or laceration of the ulnar nerve, however both the ulnar and median nerves were edematous throughout their imaged lengths, consistent with ulnar and possibly median nerve injuries.

Several days after the MRI, the patient was brought back to the OR for an exploration and release of the right ulnar nerve at the level of the elbow, forearm, and wrist, as well as transfer of the anterior interosseous nerve to the motor branch of the right ulnar nerve. Following this procedure, a slow but gradual improvement of motor and neurological function was observed.

The patient commenced targeted physical therapy at 1-month postoperative with a focus on functional improvement. Electromyography (EMG) studies were completed serially to assess recovery. Five months post-injury the motor response and sensory potential of the ulnar nerve was absent. Repeat EMG studies nine months post-injury showed improvement, with small motor responses from ulnar motor innervated muscles obtained as well as small ulnar sensory responses, which previously were absent. Further EMG studies were completed at 12- and 18-months post-injury, showing improvement in motor response and the patient had improved clinically with better strength and function. At 18-month follow-up the patient reported improved ability to grip objects and lower likelihood of dropping things. However, there was no further improvement in ulnar sensory response and the patient has ongoing paresthesia in the fourth and fifth digits of the right hand. Persistent neuropathic pain symptoms continue to be well managed with Gabapentin 600mg PO TID.

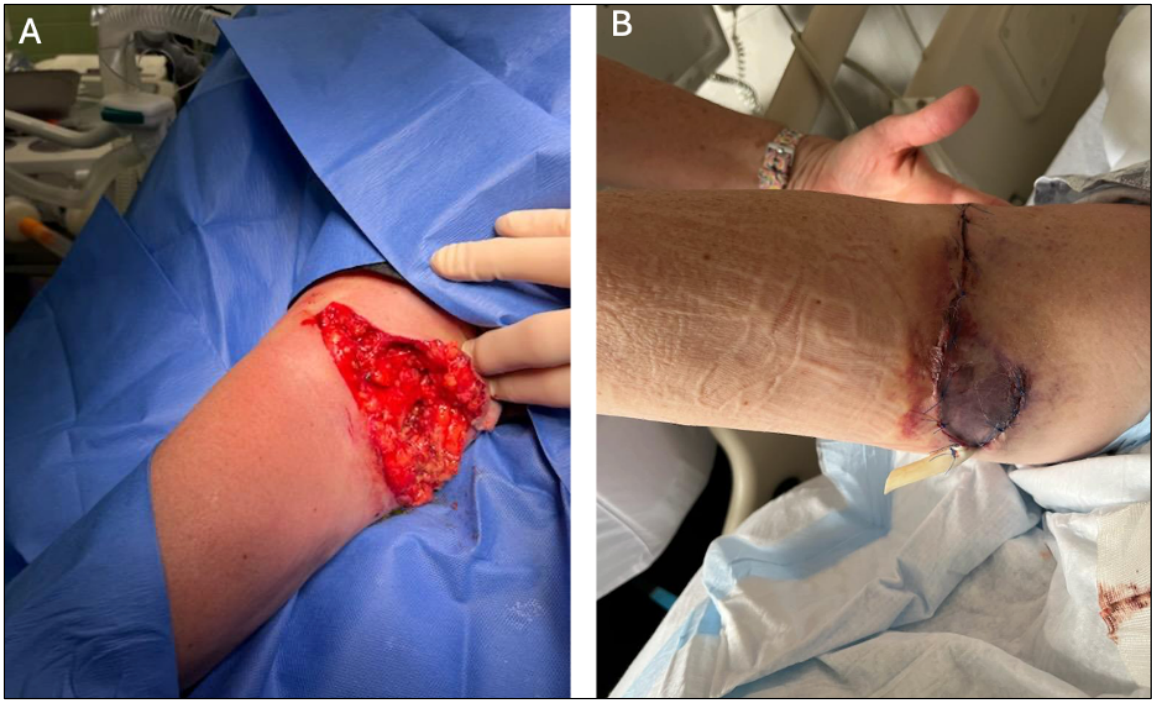


**Figure 4.** Photographs taken in the operating suite: A) Laceration following removal of ATV Handlebars. B) Laceration with visible Penrose drain following primary closure.

## DISCUSSION

The documented case is a unique presentation of penetrating upper limb trauma following an ATV rollover at low speed that resulted in complex and delayed outcomes when considering the prolonged recovery course and residual symptomatology. Incidence of ATV accidents are increasing and can result in considerable morbidity and mortality, particularly following rollover accidents as riders are unrestrained with highly variable posture and positioning.[5] Although the majority of rollover ATV accidents occur at relatively low speeds, such occurrences can still result in significant injury despite riders wearing protective equipment, such as helmets.[1,5] A recent retrospective review by Siman-Tov et al. (2020) found ATV users were more likely to suffer severe injuries than any other form of motor vehicle accident with increased use of hospital resources including surgery, ICU admissions, and prolonged length of stay.[1] Various blunt and penetrating injuries resultant from ATV-associated accidents have been reported in recent literature, including but not limited to, traumatic brain injuries, lung herniation, globe dislocation and optic nerve avulsion as well as laceration of intrabdominal structures.[6–9]

Penetrative injuries are known to occur during ATV accidents and can occur even with blunt objects such as the end of an ATV handlebar.[10] Despite the evident increase in ATV accidents, there has been limited reporting of prior penetrating trauma with resultant nerve injury. Upper extremity nerve injuries following trauma are relatively uncommon and are seen in approximately 3 – 4% of upper limb presentations to EDs.[11,12] Ulnar nerve traumas are associated with particularly poor prognosis regardless of the level of injury when compared with that of the median or radial nerve. Specifically, injuries sustained at or above the elbow level exhibit the worst prognosis, even after attempted repair.[12,13] Such findings are attributable to the role of the ulnar nerve in innervations to intrinsic muscles of the hand responsible for a wide array of motor functioning and daily tasks.[13,14]

The characteristic claw hand deformity seen in the present case was concerning for the ulnar nerve laceration, which is associated with a particularly poor prognosis, compared to a neuropraxia, the most minor form of nerve injury.[15] Despite the absence of significant ulnar nerve trauma on undertaken imaging, the outcome for this patient was complex and delayed associated with residual symptoms at approximately 18 months post-operatively and despite the use of neuropathic medication. Other reports have found the use of advanced imaging techniques, such as CT angiography to be useful in penetrative trauma with wooden foreign bodies but there was difficulty in commenting on vascular injury in this case using CT angiography with a metal foreign body.[10] Due to limitations in resources, including advanced imaging techniques and sub-specialty care, rural EDs in collaboration with their tertiary care colleagues could consider developing streamlined pathways for advanced imaging of penetrative traumas or consider early transfer to a tertiary care centre for definitive management.

Finally, ATV use in NL has increased substantially in the past two decades, which has been causally linked to rural residence.[3] Significant to this increase in usage, NL has been found to have the highest rate of ATV associated mortality in Atlantic Canada, prompting the need for greater examination of ATV safety and guidelines.[2] Several groups have studied Crush Protection Devices (CPDs), which are intended to reduce injury by decreasing significant contact between an inverted ATV and rider.[5,16] NL currently has no regulations requiring CPD usage for ATVs. In the absence of CPDs, penetrating injuries are more likely to occur when riders are thrown from the vehicle and come into contact with the vehicle or surrounding objects. Penetrative traumas and impalement injuries have been reported in the literature and present a complicated diagnostic and management dilemma, particularly in rural environments where resources are limited, and sub-speciality care and advanced imaging modalities are unavailable.[8,10] Future studies could consider evaluating the effectiveness of CPDs in reducing the risk of contact injuries between inverted ATVs and riders.

## CONCLUSIONS

Trauma sustained while operating recreational ATVs are becoming an increasingly common presentation to rural EDs. We have reported a unique case of upper extremity penetrating trauma that has important implications in the consideration of management pathways from these traumatic injuries while highlighting the need for further examination of ATV safety.

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# Being Human in Medicine

## Family, Health, Medicine

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We each have unique stories that have shaped us into who we are today and will impact the physicians we will become. I am from the small town of Random Island, Newfoundland, and Labrador. Following a degree in Recreation, Master's in Kinesiology, and almost a decade in the fitness industry working with healthy, ill, injured, athletic, and military populations, I was accepted into medicine at 29 after three attempts. Medicine is something I have always been passionate about. Reflecting, I think I delayed applying because I did not want to feel like a failure if I did not get accepted. Now, I realize the only failure is not going after what is important. I entered medical school with a girlfriend, 10-year-old stepdaughter, and week-old twins. I have a lot of responsibilities that humble and motivate me to be the best version of myself. I hope that sharing some of my story and personal perspectives about how I approach life and try to manage medicine, a family, and a healthy lifestyle offers some comfort, perspective, and inspiration into what it means to be human in medicine.

Being human in medicine starts with remembering the human condition. While the scientific and spiritual communities can debate what it means to be human, I have some ideas. In essence, it means *memento mori*, or in other words, we live and will eventually die, no exceptions. This humbling fact reminds us of the finite time we have and urges us to be deliberate about the life we want to live. Being human also means we think, have beliefs and emotions, make choices, and grow. We are far from perfect. It makes us the same (humans) but different (individuals). We can acknowledge the past, live in the present, and build the future. We are responsible for our lives and yet vulnerable to immense uncertainty.

Medicine and helping people gives us pride, purpose, and fulfillment. We happily justify committing our entire lives to it knowing there will be sacrifices in other areas of our lives. Medicine rewards hard work and excellence, rebukes mistakes and complacency, and humbles knowledge and overconfidence. We put high expectations on ourselves, and others put high expectations on us. Our decisions have consequences on people's lives. Medicine grooms us to embrace the grind and never settle. It is a requirement to succeed. Once we become accustomed to it, it is hard to dial it back. Part of being human is the ability to pursue, but also the necessity to rest and experience other aspects of life. If we don't, we will burn out or let our lives pass, not realizing what we've missed.

When I think about being human in medicine, I try to take a step back and regularly reflect on what I want from my life, what is in my control, what is most important, and how to prioritize and take appropriate action. I want to live a long, healthy, happy, productive, purposeful, and fulfilled life and leave the world a better place than when I found it. It is simple but resonates with me and gives me direction. I also need to be cognizant of what is within my control because many things are not. Focusing on what I can control allows me to stress less about the things that I cannot, live happier, and feel more in control. Letting go and accepting what I cannot control allows me to focus on less, which allows me to put more effort into what is most important. I have three main important categories in my life: my family, health, and career, in that order. Looking back from my deathbed gives me this perspective. Above all, I want to be a good partner and father – being present, available, and sharing the family experience. Secondly, I want to take care of my health. Finally, my career as a future physician.

Understanding this hierarchy is important because without it, we can get lost. There have been many times I have put academics ahead of family and health. Straying from one's values is easy to do because of the passion and demand for medicine. I can put 100 hours into it every week and still have endless things to learn. Medical school is demanding and requires hard work, but I don't think the excessive overwhelming stress is worth your family or health. Thankfully, I have a family, body, and systems in place that center me when my priorities are out of alignment. With all this in mind, the final piece is figuring out how to structure my life to align with my goals and navigating everything life throws at me.

Figuring out what works as an individual is essential. Scheduling, measuring, and compartmentalization work for me. I treat my academics like an extended workweek allocating Monday to Saturday 9 am to 6 pm, mostly at MUN. Studying at home is not as efficient and makes it

harder to create mental space. When a due date is close, I may go over time, but I am conscious of getting it back when things slow down. I log my weekly hours to create this accountability. This routine allows me to compartmentalize time for family, health, or other things. By putting in more hours I would perform better, but using my values as a guide makes decisions easier. I am not willing to sacrifice my family or health to an extreme degree. Most of my time outside academics is for my family. I try to be fully present, which usually includes putting my phone or laptop away and trying to participate in shared activities. I put a lot of time into my mental and physical health because it impacts everything else. Health truly is wealth. I categorize five main factors of health that come from Ben Bergeron's podcast, *Chasing Excellence*, plus one that I added, Planet. They are mindset, exercise, nutrition, recovery, and connection.

I think of Mindset as how we think. It determines why we live the way we do. It is like Gandhi said, "Your beliefs become your thoughts, your thoughts become your words, your words become your actions, your actions become your habits, your habits become your values, your values become your destiny". If we can influence our minds to think happy, growth-minded, and morally good, we give ourselves a better chance to live a good life. It is a trainable skill. I consciously train it by trying to be self-aware and learning, every day. It usually manifests as reading 30 minutes of something non-fiction each day that improves me as a human being. In terms of fitness, I aim for 60 minutes of moderate to high-intensity physical activity six times per week. I created a non-negotiable for myself as I struggled to exercise when balancing school and family. One missed day becomes a recovery day, and extra effort goes into the next day. If I miss a second day, it becomes non-negotiable the third. I also purchased a treadmill and home gym to increase accessibility and reduce travel time. I watch lectures while on the treadmill allowing me to combine study and exercise without having to cut into family time.

For nutrition, I keep it simple. Maintaining a healthy diet is difficult in medical school and with a young family, but strategies exist. I follow the 'eat real food, not too much, mostly plants' philosophy of Michael Pollan. I try and buy healthy food, meal prep, and use a meal delivery service a couple of times a week. I think of recovery as our mental and physical battery that we use daily for everything and need to recharge. I consider sleep the most important recharger, aiming for eight hours per night (56 per week). With babies who wake up nightly, I take naps when possible.

Connection simply refers to the strong meaningful connections we have in our lives. It can be to family, friends, pets, career, purpose, community, or others and is what makes life worth living. Quality matters more than quantity. I try and connect with my career and peers at school, my family at home, and my friends at least once a week. I often combine fitness and connection by playing team sports or working out in groups.

The final factor is the planet. Human connection to nature is a core component of being human, even in our increasingly modernized world. It is no secret the role nature has in supporting or destroying life. While far from perfect, I make the effort to try and educate myself and take action to reduce, reuse, and recycle to help our planet because it impacts me, my family, my community, the world, and the future.

The six factors act like a compass to help navigate my daily life in the direction I want to go while accepting the uncontrollable events that occur, and the strengths and weaknesses of being human in medicine.

I would summarize being human in medicine into a few simple concepts. We need to accept the human condition and acknowledge the strengths and weaknesses that come with it. We need to take accountability for doing the best we can to live based on what is important to us, understanding that moving in the right direction is more important than perfection. Within medicine, we need to remember that our time and energy are limited, and we need to take care of ourselves, to take care of others, and live long, healthy, happy lives.

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