Problem Description

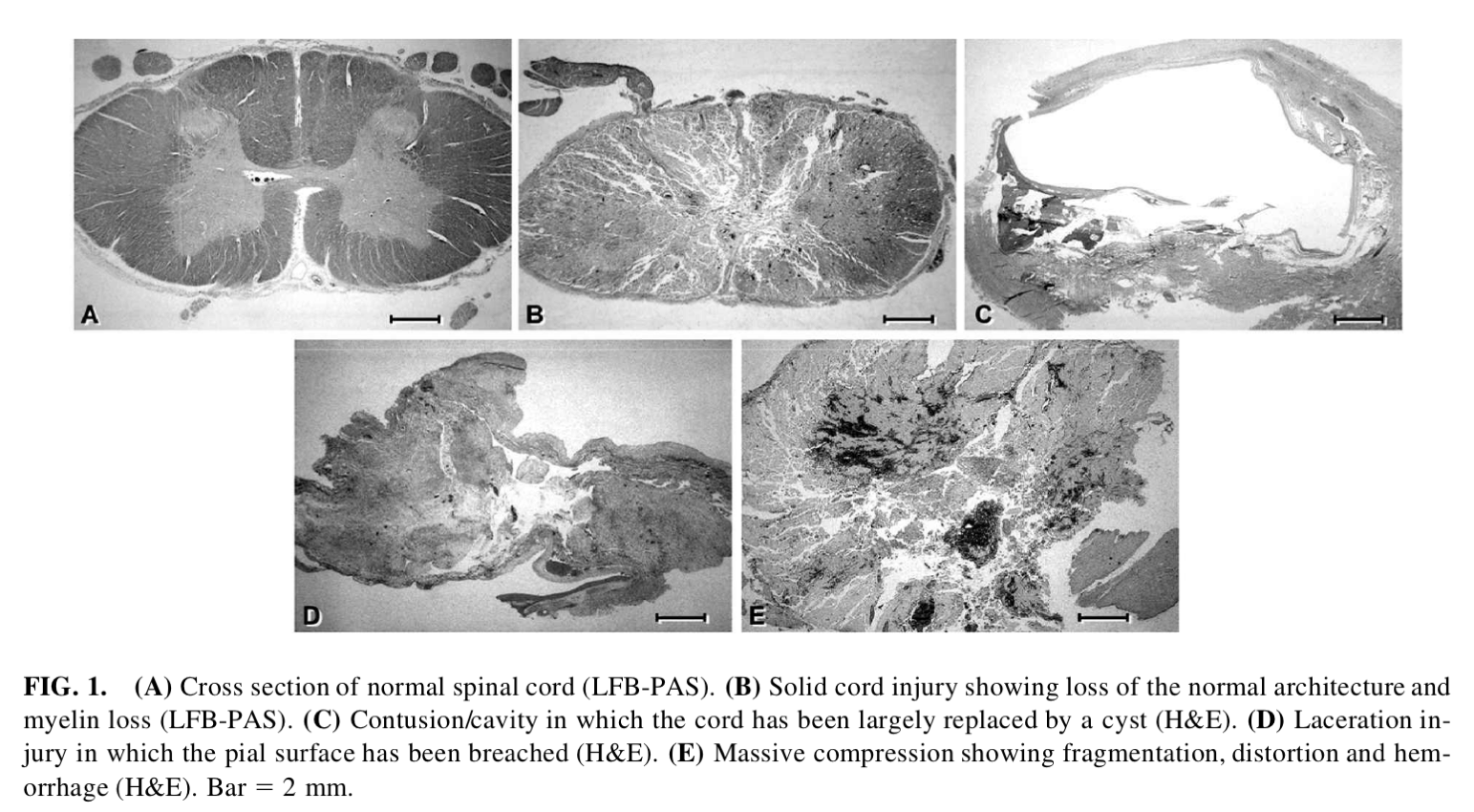
Traumatic spinal cord injury (SCI) is a debilitating neurological condition with severe socioeconomic impact on the health care system. Since 2015, about 30% of persons with SCI are re-hospitalized for disease of the skin, or respiratory, digestive circulatory, and musculoskeletal diseases[[1]](#footnote-2). There are approximatively 54 new cases of SCI per one million people (17,730 new cases)[[2]](#footnote-3). The injured individuals are predominantly male. The age distribution is bimodal with a first peak involving young adults and a second peak for adults over the age of 60. Injuries in this last group, usually result from falls and these patients have worst outcomes than younger patients. More than 90% of SCI cases are traumatic such as traffic accidents, violence, sports or falls (**Figure 1** below). Incomplete tetraplegia is the most frequent neurological outcome (**Figure 2** below). The estimated lifetime costs average 1 to 5 million per individual[[3]](#footnote-4).

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| **Figure 1: Cause** |
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| **Figure 2: Neurological Level** |
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Source: National spinal cord injury statistical center

SCI are mostly contusion (49% of cases), or lacerations (21%) cases. Compression shows no breach or disruption in the surface anatomy, and presents areas of hemorrhage and necrosis. In contrast, laceration results in clear-cut of the spinal cord, the lesions are dominated with collagenous connective tissue. In massive compression, the cord is pulpified to a varying degree with extensive fibrous scarring[1].

**Figure 3: “The Pathology of Human Spinal Cord Injury: Defining the Problems”**

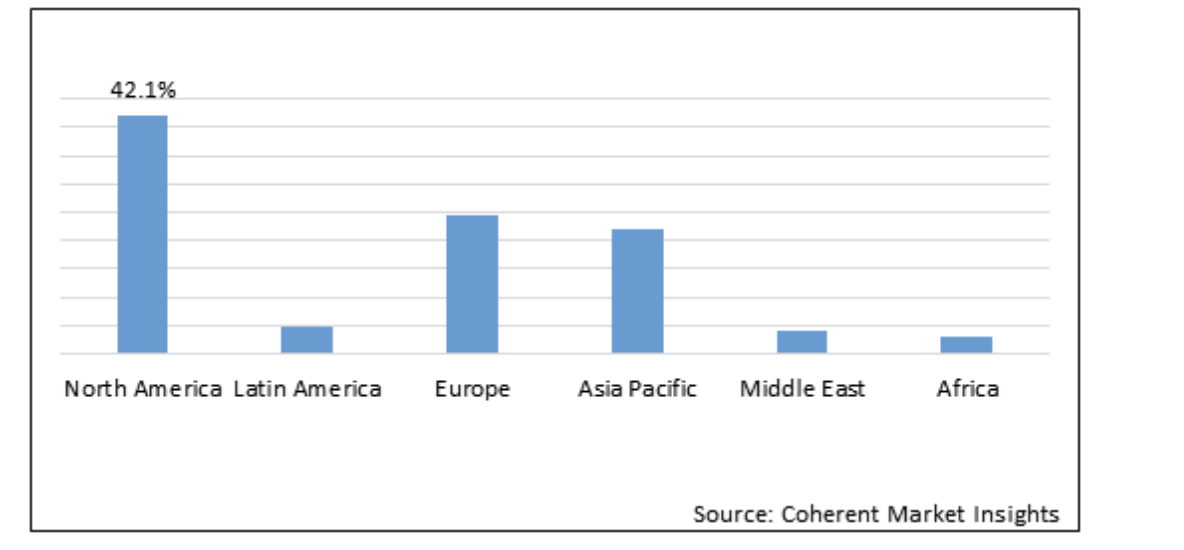


The initial primary injury causes neuronal death (axons and oligodendrocytes), increase in the level of pro-inflammatory cytokines, and recruits inflammatory cells, such as macrophages, neutrophils and lymphocytes in the spinal cord, demyelination, ischemia and hypoxia. This process persists for weeks and initiates a second wave of apoptosis in neurons and oligodendrocytes. In the late phase (weeks to months/years), the injured tissue is isolated from the environment by reactive astrocytes through the formation of a mesenchymal scar. This phase is also characterized by developments of cysts, and syrinx, and Schwannosis [1] (**Figure 4 and 5** below).

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| **Figure 4: Norenberg et al.**  **Pathophysiology of traumatic. SCI** | **Figure 5: [2]**  **Main cellular targets of cell therapy in SCI** |
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Motivation

According to Coherent Market Insight, the spinal cord injury therapeutic market is estimated to be valued at USD 6.7 million in 2021 and is expected to have a compound annual growth rate (CAGR) of 5.1% to reach USD 9.6 million in 2028. North America represents the largest market with 42.1%.



Neuro-Spinal graft targets patients who have suffered a thoracic AIS (American Spinal Injury Association Impairment scale) A traumatic spinal cord injury at neurological level of injury of T2-T12. Compared to a neurological “incomplete” injury (AIS-B, C or D), AIS-A has the least potential improvement, the lowest lifetime survival [3](**Figure 6** below). In term of costs, Medicaid is the only national program covering services that SCI survivors require. Mean annual cost oof hospitalization are the highest among persons with AIS-A, AIS-B, or AIS-C injuries with a daily cost of $2601 (2015 US$) [3] (**Figure 7** below).

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| **Figure 6: ASIA Impairment Scale Grade** | **Figure 7: Estimated lifetime expectancy** | |
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In the first clinical trial, conducted by Lineage, OPC1, oligodendrocytes progenitor cells, were injected to individuals with a neurological level of injury between T3 and T11 and with AIS-A. After 10-year follow-up the trial no serious adverse events (SAEs) were reported. In a second trial, escalating doses were administered to 33 participants. No SAEs reported were related to OPC1, 22 participants attained a one-motor-level improvement and 7 attained a two-motor-level improvement on one side of the body.

**References**:

[1] M. D. Norenberg, J. Smith, and A. Marcillo, “The Pathology of Human Spinal Cord Injury: Defining the Problems,” *Journal of Neurotrauma*, vol. 21, no. 4, pp. 429–440, Apr. 2004, doi: 10.1089/089771504323004575.

[2] J. Desai, S. Steiger, and H.-J. Anders, “Molecular Pathophysiology of Gout,” *Trends in Molecular Medicine*, vol. 23, no. 8, pp. 756–768, Aug. 2017, doi: 10.1016/j.molmed.2017.06.005.

[3] E. M. Dukes, S. Kirshblum, A. A. Aimetti, S. S. Qin, R. K. Bornheimer, and G. Oster, “Relationship of American Spinal Injury Association Impairment Scale Grade to Post-injury Hospitalization and Costs in Thoracic Spinal Cord Injury,” *Neurosurgery*, vol. 83, no. 3, pp. 445–451, Sep. 2018, doi: 10.1093/neuros/nyx425.

1. National spinal cord injury statistical center. [↑](#footnote-ref-2)
2. Jain NB, Ayers GD, Peterson EN, et al. Traumatic spinal cord injury in the United States, 1993-2012. JAMA. 2015;313(22):2236-2243. [↑](#footnote-ref-3)
3. Economic Impact of SCI published in the journal Topics in Spinal Cord Injury Rehabilitation, Volume 16, Number 4, in 2011. [↑](#footnote-ref-4)