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Original Article

Optimality quality control thresholds for effective management of multiple sclerosis

Kalpana Polisetty[1*] and Tirupathi Rao Padi[2]

[1] *Department of Sciences and Humanities, Vignan's Foundation for Science, Technology and Research, Vadlamudi, Guntur, 522213 India*

[2] *Department of Statistics, Pondicherry University, Kalapet, Puducherry, 605014 India*

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Abstract

Multiple Sclerosis (MS) is a chronic disease of the nervous system that affects various parts of the body through its neuro signal impulses. This study focused on the development of quality control thresholds for the optimal health management of the MS disease. With the help of mean and variance from stochastic models of MS, the thresholds for quality assurance at the upper and lower limits of MS causing cells and oligodendrocytes are developed. Sampling distributions of simulated data were used to get the control limits. These control limits will act as guiding alerts used in designing quality specifications and health-care decision support systems. The analysis is carried out with threshold limits at a required level of significance by considering natural tolerances.

Keywords: multiple sclerosis, sampling distributions, quality control thresholds, healthcare management, simulation techniques

1. Introduction

MS is an unpredictable disease that affects the central nervous system (CNS). It is a demyelinating disease caused by the immune system. It spoils the protective sheath (myelin) that covers the axon of nerve fibers. Myelin is a coating acting like the insulation on copper/aluminum metal in electrical wires. Degrading the myelin coating will damage the functionality of nerve cells, leading to passive, slow or even fully inhibited communications within the CNS. The effects of MS are severe, with long term damage/deterioration of the nervous system harming both the body and the brains. The neuronal impulses in MS patients can show prominent symptoms of this disease, but the level of damage in the nerves varies widely from person to person. Symptoms typically include vision loss, walking difficulties, numbness, and paralysis. The reasons for getting MS are not clear, and the symptoms can be diverse and confusing: their emergence need not follow a specific pattern, and it is difficult to diagnose MS even today. The symptoms are due to the loss of signal transmission within the nerve systems that includes brain and spinal cord. It is not certain whether the immune system triggers the problem of MS. The stochastic nature of several factors in the survival mechanisms of the body that interact with emergence of MS is a matter of interest to the researchers. Both genetic and environmental factors may be involved in the development of MS (Compston & Coles, 2008).

Several factors influence the risk of MS. Any person in the age group from 16 to 55 years has some likelihood of getting it. Females have 2 to 3 fold higher risk than males. Hereditary component is indicated by the family history correlating with individual risk. Specific infections by a variety of viruses can increase vulnerability to MS. The white human race is geographically located in predominantly temperate climatic conditions, and has a higher risk than the other human subpopulations; reduced exposure to sunlight and low levels of vitamin D seem to increase the risk of MS. Diseases linked with the endocrine system, such as diabetes, thyroid, inflammatory bowel disease, etc., also significantly impact the

*Corresponding author
Email address: drtrpadi@gmail.com

risk of getting this disease (Cullen, Robyn, & Bruce, 2012; Goodin, 2009). The MS condition of a patient is classified by its level of severity. The commonly used levels are (i) Clinically Isolated Syndrome (CIS) with first interlude of neurological symptoms for at least 24 hours; (ii) Relapse-Remitting MS (RRMS) that is the most common and general disease form (around 85% of the people diagnosed with MS); and with more often occurring attacks and new/increasing symptoms there are (iii) Secondary Progressive MS (SPMS) after initial episodes or relapse and remission, as the disease progresses steadily; and (iv) Primary Progressive MS (PPMS) with symptoms that worsen progressively, without early relapses or remissions. Around 15% cases suffering from the last mentioned category of MS. These categories inform about the severity of the disease and how the treatment will work (Ingrid, & Rock, 2011; Tanja, Gueanelle, Andreas, Jana, & Wollfgang, 2002). Even though there is no cure for MS, effective treatment can speed up the recovery from attacks, modify the course of the disease, help manage the symptoms, etc., and it can be planned with healthcare takers.

Statistical quality control charts can be applied in the monitoring of MS treatments. They can provide adequate tools to assess the performance of healthcare management. Various analytical procedures are under consideration for the rational interpretation of MS status. The evaluation of medical data is primarily focused on statistical quality control tools to monitor the output of the healthcare system (Knapp & Miller, 1983). Statistical quality control charts are constructed and applied for monitoring the blood glucose levels (Oniki, Clemmer, Arthur, & Linford, 1995). Various statistical quality control tools and statistical process control have been used in healthcare studies (Benneyan, Lioyd, & Plsek, 2003). Various studies of surgical and interventional procedures have applied CUSUM charts from quality control (Biau, Resche-Rigon, Godiris-Petit, Nizard, & Porcher, 2007). Growth and loss of MS cells and oligodendrocytes were studied by constructing bivariate stochastic models and by deriving statistics characterizing the developed probability models (Tirupathi Rao, Kalpana, & Rajasekhar, 2012*)*. Optimization models were developed for minimizing the severity of MS by exploring the parameters and monitoring the health management of MS (Tirupathi Rao, Kalpana, & Kiran, 2013*)*. The combined effect of the sizes of MS cells and oligodendrocytes have been considered in developing the optimization problems to control the growth of MS (Kalpana, Tirupathi Rao, & Rajasekhar, 2014*)*. The advent of new MS therapies and evolving management strategies offered exciting new opportunities to optimize treatment outcomes (Tjalf *et al.*, 2016). Effective and strategic interventions were proposed for prompt, optimal treatment and switching strategy of therapy for patients with suboptimal responses or treatment failures with their current MS treatment (Tjalf & Katja, 2017).

All the above reported research studies have emphasized the development of stochastic models and optimization methods for MS cells and oligodendrocytes. However, there is a little prior work on developing statistical quality/ process control approaches to the health status of MS disease. The average sizes and variances of MS causing cells as well as of oligodendrocytes are indicators used in these research studies. The core objective of this current study is to provide the guiding principles on the warranted levels of both MS cells and oligodendrocytes. The study applies both stochastic models and optimization methods for further use in the user interface to therapies. This study also aimed to design the quality specifications for healthcare decision support systems for the optimal management of MS.

2. Quality Control Devices on MS Causing Cells and Oligodendrocytes

The current study focused on the development of quality control devices through the control limits for both standard and volatility measures, based on means and variances of MS and oligodendrocytes. The statistical measures used in this study for developing the control limits were derived by the same researchers in their previous works on stochastic modelling of MS causing cells along with the sizes of oligodendrocytes (Kalpana, Tirupathi Rao, & Rajasekhar, 2014). The quality control devices standard (mean) and variability (standard deviation) were obtained from the above mentioned prior study.

2.1 Notation and Terminology

Based on Kalpana, Tirupathi Rao, and Rajasekhar (2014), the results of that study are utilized with the following notation and terminology.

X: Number of MS cells
Y: Number of oligodendrocytes
a_i: The Mean size of MS cells at i^{th} point of time; i= 1,2, ...,k
b_i: The average size of oligodendrocytes at i^{th} point of time; i= 1,2, ...,k
k: Number of sample groups
λ_1 & λ_2: Growth rates of MS and oligodendrocytes, respectively
μ_1 & μ_2: Loss rates of MS and oligodendrocytes, respectively
I_0 & J_0: Initial sizes of MS & oligodendrocytes
$m_{1,0}(t)$ & $m_{0,1}(t)$: means of MS and oligodendrocytes, respectively
$m_{2,0}(t)$ & $m_{0,2}(t)$: variances of MS and oligodendrocytes, respectively

2.2 Control limits for mean and volatility chart of MS causing cells

As $a_1 = e^{[\lambda_{11}-\mu_{11}]t_1} I_0, a_2 = e^{[\lambda_{12}-\mu_{12}]t_2} I_0, ..., a_k = e^{[\lambda_{1k}-\mu_{1k}]t_k} I_0$

$$E(\bar{a}) = E\left(\frac{1}{k}\sum_{i=1}^{k} a_i\right) = \frac{I_0}{k}\sum_{i=1}^{k} e^{[\lambda_{1i}-\mu_{1i}]t_i};$$

$$E(\bar{a})^2 = \frac{1}{k^2} E\left(\sum_{i=1}^{k} e^{[\lambda_{1i}-\mu_{1i}]t_i} I_0\right)^2$$

$$V(\bar{a}) = \frac{I_0^3}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{1i}+\mu_{1i}}{\lambda_{1i}-\mu_{1i}}\right] e^{[\lambda_{1i}-\mu_{1i}]t_i}\left(e^{[\lambda_{1i}-\mu_{1i}]t_i}-1\right)\right.$$

$$\left.+\left(e^{2[\lambda_{1i}-\mu_{1i}]t_i} I_0\right)\right\} - \left(\frac{I_0}{k}\sum_{i=1}^{k} e^{[\lambda_{1i}-\mu_{1i}]t_i}\right)^2$$

The control limits for mean chart of MS causing cells $= E(\bar{a}) \pm 3V(\bar{a})$

$$= \frac{I_0}{k}\sum_{i=1}^{k} e^{[\lambda_{1i}-\mu_{1i}]t_i} \pm 3\left[\frac{I_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{1i}+\mu_{1i}}{\lambda_{1i}-\mu_{1i}}\right]e^{[\lambda_{1i}-\mu_{1i}]t_i}\left(e^{[\lambda_{1i}-\mu_{1i}]t_i}-1\right)+\left(e^{2[\lambda_{1i}-\mu_{1i}]t_i}I_0\right)\right\}-\left(\frac{I_0}{k}\sum_{i=1}^{k}e^{[\lambda_{1i}-\mu_{1i}]t_i}\right)^2\right]^{1/2} \quad \ldots\ldots (2.2.1)$$

The control limits for Volatility of MS causing cells are

$$\left[\left(\frac{I_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left(\frac{\lambda_{1i}+\mu_{1i}}{\lambda_{1i}-\mu_{1i}}\right)e^{[\lambda_{1i}-\mu_{1i}]t_i}\left(e^{[\lambda_{1i}-\mu_{1i}]t_i}-1\right)+\left(e^{2[\lambda_{1i}-\mu_{1i}]t_i}I_0\right)\right\}\right)-\left(\frac{I_0}{k}\sum_{i=1}^{k}e^{[\lambda_{1i}-\mu_{1i}]t_i}\right)^2\right]^{1/2} \pm 3\left[\left(\frac{I_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left(\frac{\lambda_{1i}+\mu_{1i}}{\lambda_{1i}-\mu_{1i}}\right)e^{[\lambda_{1i}-\mu_{1i}]t_i}\left(e^{[\lambda_{1i}-\mu_{1i}]t_i}-1\right)+\left(e^{2[\lambda_{1i}-\mu_{1i}]t_i}I_0\right)\right\}\right)-\left(\frac{I_0}{k}\sum_{i=1}^{k}e^{[\lambda_{1i}-\mu_{1i}]t_i}\right)^2\right] \quad \ldots\ldots (2.2.2)$$

2.3 Control limits for mean and volatility of oligodendrocytes

As $b_1 = e^{[\lambda_{21}-\mu_{21}]t_1}J_0, b_2 = e^{[\lambda_{22}-\mu_{22}]t_2}J_0, \ldots, b_k = e^{[\lambda_{2k}-\mu_{2k}]t_k}J_0$.

$$E(\bar{b}) = \frac{J_0}{k}\sum_{i=1}^{k} e^{[\lambda_{2i}-\mu_{2i}]t_i};$$

$$E(\bar{b})^2 = \frac{J_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{2i}+\mu_{2i}}{\lambda_{2i}-\mu_{2i}}\right]e^{[\lambda_{2i}-\mu_{2i}]t_i}\left(e^{[\lambda_{2i}-\mu_{2i}]t_i}-1\right)+\left(e^{2[\lambda_{2i}-\mu_{2i}]t_i}J_0\right)\right\}$$

As $V(\bar{b}) = E(\bar{b})^2 - \left[E(\bar{b})\right]^2$, substitute $E(\bar{b})$ and $E(\bar{b})^2$ in $V(\bar{b})$, we have

$$V(\bar{b}) = \frac{J_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{2i}+\mu_{2i}}{\lambda_{2i}-\mu_{2i}}\right]e^{[\lambda_{2i}-\mu_{2i}]t_i}\left(e^{[\lambda_{2i}-\mu_{2i}]t_i}-1\right)+\left(e^{2[\lambda_{2i}-\mu_{2i}]t_i}J_0\right)\right\}-\left(\frac{J_0}{k}\sum_{i=1}^{k}e^{[\lambda_{2i}-\mu_{2i}]t_i}\right)^2$$

The control limits for mean chart of oligodendrocytes $= E(\bar{b}) \pm 3V(\bar{b})$

$$= \frac{J_0}{k}\sum_{i=1}^{k} e^{[\lambda_{2i}-\mu_{2i}]t_i} \pm 3\left[\frac{J_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{2i}+\mu_{2i}}{\lambda_{2i}-\mu_{2i}}\right]e^{[\lambda_{2i}-\mu_{2i}]t_i}\left(e^{[\lambda_{2i}-\mu_{2i}]t_i}-1\right)+\left(e^{2[\lambda_{2i}-\mu_{2i}]t_i}J_0\right)\right\}-\left(\frac{J_0}{k}\sum_{i=1}^{k}e^{[\lambda_{2i}-\mu_{2i}]t_i}\right)^2\right]^{1/2} \quad \ldots\ldots (2.2.3)$$

The control limits for volatility of oligodendrocytes are

$$= \left[\frac{J_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{2i}+\mu_{2i}}{\lambda_{2i}-\mu_{2i}}\right]e^{[\lambda_{2i}-\mu_{2i}]t_i}\left(e^{[\lambda_{2i}-\mu_{2i}]t_i}-1\right)+\left(e^{2[\lambda_{2i}-\mu_{2i}]t_i}J_0\right)\right\}-\left(\frac{J_0}{k}\sum_{i=1}^{k}e^{[\lambda_{2i}-\mu_{2i}]t_i}\right)^2\right]^{1/2} \pm 3\left[\frac{J_0^{\,3}}{k^2}\sum_{i=1}^{k}\left\{\left[\frac{\lambda_{2i}+\mu_{2i}}{\lambda_{2i}-\mu_{2i}}\right]e^{[\lambda_{2i}-\mu_{2i}]t_i}\left(e^{[\lambda_{2i}-\mu_{2i}]t_i}-1\right)+\left(e^{2[\lambda_{2i}-\mu_{2i}]t_i}J_0\right)\right\}-\left(\frac{J_0}{k}\sum_{i=1}^{k}e^{[\lambda_{2i}-\mu_{2i}]t_i}\right)^2\right] \quad \ldots\ldots (2.2.4)$$

3. Data Analysis and Discussion

In this section, an attempt is made for understanding the evaluation protocols of health status with numerical illustrations. The numerical data are obtained from simulations using the software MATHCAD version 7.0. Here, the control limits are calculated by using the concept of natural tolerance.

With regard to Table 1, the calculated means at various time points of MS causing cells are 8.91, 6.38, 9.2, 8.17, 5.14, 6.9, 5.37, 6.47, 5.84, 4.96, 6.12, 5.23, 7.43, 4.62, and 6.96; sample size (n)=8; overall mean $E(\bar{X})$=6.51; overall standard deviation (S.D.)=3.97; control limits of mean chart are at $E(\bar{X})\pm 3S.E(\bar{X})$, which provides the Upper Control Limit $(UCL_{\bar{x}})$ as 10.72, and the Lower Control Limit $(LCL_{\bar{x}})$ as 2.31, and Central Limit $(CL_{\bar{x}})$ as 6.51. Based on these results the control chart for Mean of MS causing cells is constructed, and is shown in Figure 1. From Figure 1, it is observed that the process of average number of MS causing cells is under control.

From Table 2 the calculated standard deviations (S.D) at various time points of MS causing sells are 4.89, 3.92, 5.54, 4.66, 4.19, 4.88, 3.08, 3.62, 4.02, 3.08, 3.92, 3.06, 3.35, 3.12 and 2.86. Sample size (n)=8; $E(S)=3.88$ and $V(S)=15.74$; control limits for 'S' chart are 3.88±15.74(0.5); the UCL= 3.88+15.74(0.5)=11.75; the LCL=3.88-15.74(0.5)= -3.99, since $\sigma_x \geq 0$ then LCL=0 and CL=3.88. Based on these observations the control chart for volatility of MS causing cells was developed and is shown in Figure 2. This figure shows that the process quality on volatility of MS causing cells is under control.

Table 1. The expected number of MS causing cells $E(a_i)$ at different time periods.

λ_{1i}	μ_{1i}	t	$E(a_i)$	λ_{1i}	μ_{1i}	t	$E(a_i)$	λ_{1i}	μ_{1i}	t	$E(a_i)$	λ_{1i}	μ_{1i}	t	$E(a_i)$	λ_{1i}	μ_{1i}	t	$E(a_i)$
1.9	0.3	1.0	7.9	1.5	0.5	2.0	10.3	1.7	1.7	3.0	1.5	2.5	1.9	4.0	14.4	2.4	2.4	5.0	1.5
2.6	0.3	1.0	16.6	1.3	1.4	2.0	1.5	1.9	1.2	3.0	11.9	2.5	1.9	4.0	13.9	2.4	2.1	5.0	6.2
1.7	0.3	1.0	6.4	1.7	0.9	2.0	7.5	2.2	1.6	3.0	8.3	2.1	2.2	4.0	1.1	2.4	2.1	5.0	9.2
2.7	0.6	1.0	13.1	1.9	1.9	2.0	1.5	2.0	1.5	3.0	7.6	2.6	2.2	4.0	9.7	2.5	2.5	5.0	1.5
1.9	0.2	1.0	8.8	1.1	0.2	2.0	11.1	2.0	2.0	3.0	1.5	2.6	2.3	4.0	5.3	2.0	2.0	5.0	1.5
1.8	0.2	1.0	5.0	0.9	0.2	2.0	4.1	2.5	1.8	3.0	13.1	2.6	2.3	4.0	4.7	2.4	2.1	5.0	7.9
2.2	0.2	1.0	12.2	0.9	0.4	2.0	5.0	1.6	0.8	3.0	16.6	2.6	2.1	4.0	10.1	1.9	1.9	5.0	1.5
1.9	2.1	1.0	1.3	1.1	0.2	2.0	10.1	1.5	0.8	3.0	13.1	2.9	2.5	4.0	6.2	1.8	1.4	5.0	11.8
2.2	1.8	6.0	12.3	2.5	2.2	7.0	9.9	2.3	2.1	8.0	6.2	2.8	2.8	9.0	2.5	3.3	3.2	10.0	4.4
2.2	1.9	6.0	10.3	2.5	2.3	7.0	6.5	2.3	2.1	8.0	7.9	2.8	2.7	9.0	7.4	3.4	3.2	10.0	10.7
2.2	1.9	6.0	11.6	2.7	2.5	7.0	5.6	2.4	2.2	8.0	6.8	2.6	2.5	9.0	3.9	3.1	3.0	10.0	4.8
1.6	1.6	6.0	1.4	2.7	2.7	7.0	1.5	2.2	1.9	8.0	11.8	2.9	2.9	9.0	1.5	3.4	3.4	10.0	1.3
1.9	1.6	6.0	6.8	2.0	2.0	7.0	1.6	2.1	2.1	8.0	1.5	2.9	2.9	9.0	1.3	3.0	2.8	10.0	7.9
1.9	1.6	6.0	10.3	2.0	1.9	7.0	3.2	2.3	2.1	8.0	8.6	2.9	2.7	9.0	11.6	2.8	2.8	10.0	2.4
2.1	2.1	6.0	1.3	2.2	2.0	7.0	8.6	2.1	2.1	8.0	1.1	2.8	2.6	9.0	8.9	3.3	3.2	10.0	5.3
2.2	2.2	6.0	1.3	2.3	2.1	7.0	6.1	2.4	2.2	8.0	7.9	2.1	2.1	9.0	9.7	3.2	3.1	10.0	2.9
3.2	3.1	11.0	3.9	2.6	2.5	12.0	9.7	2.5	2.4	13.0	8.7	2.3	2.1	14.0	9.9	1.6	1.5	15.0	7.2
3.4	3.2	11.0	7.5	2.5	2.5	12.0	2.3	2.6	2.5	13.0	6.7	2.1	2.1	14.0	1.4	1.6	1.5	15.0	9.7
3.2	3.2	11.0	1.4	2.5	2.4	12.0	4.7	2.6	2.4	13.0	8.7	2.2	2.1	14.0	2.4	1.5	1.4	15.0	9.7
3.2	3.1	11.0	6.7	2.7	2.6	12.0	6.0	2.6	2.5	13.0	11.3	2.3	2.2	14.0	7.5	1.5	1.4	15.0	8.3
3.4	3.3	11.0	6.0	2.6	2.6	12.0	1.3	2.6	2.5	13.0	5.2	2.2	2.2	14.0	4.9	1.5	1.5	15.0	1.0
3.5	3.3	11.0	14.4	2.5	2.5	12.0	2.6	2.5	2.5	13.0	1.1	2.2	2.2	14.0	1.2	1.5	1.4	15.0	8.3
3.3	3.2	11.0	6.0	2.6	2.5	12.0	8.6	2.5	2.4	13.0	6.7	2.2	2.2	14.0	3.2	1.6	1.5	15.0	5.3
3.3	3.3	11.0	3.1	2.6	2.4	12.0	6.8	2.5	2.3	13.0	11.3	2.6	2.5	14.0	6.5	1.6	1.5	15.0	6.2

Table 2. Summary of the expected number of MS causing cells.

S. No.	t_1=1	t_2=2	t_3=3	t_4=4	t_5=5	t_6=6	t_7=7	t_8=8	t_9=9	t_{10}=10	t_{11}=11	t_{12}=12	t_{13}=13	t_{14}=14	t_{15}=15
1	7.92	10.28	1.46	14.44	1.52	12.31	9.88	6.23	2.51	4.35	3.86	9.68	8.67	9.88	7.17
2	16.61	1.51	11.94	13.87	6.17	10.28	6.49	7.93	7.39	10.70	7.46	2.29	6.69	1.39	9.68
3	6.42	7.46	8.33	1.07	9.21	11.59	5.64	6.75	3.94	4.81	1.43	4.71	8.67	2.44	9.68
4	13.07	1.51	7.61	9.68	1.45	1.42	1.49	11.82	1.46	1.31	6.69	5.99	11.25	7.46	8.33
5	8.76	11.13	1.51	5.31	1.52	6.75	1.60	1.48	1.34	7.93	5.99	1.26	5.16	4.90	1.02
6	5.00	4.06	13.07	4.71	7.93	10.28	3.22	8.59	11.59	2.39	14.44	2.59	1.08	1.21	8.33
7	12.18	5.00	16.61	10.07	1.52	1.34	8.59	1.07	8.85	5.31	5.99	8.59	6.69	3.22	5.31
8	1.31	10.07	13.07	6.23	11.82	1.26	6.05	7.93	9.68	2.92	3.10	6.75	11.25	6.49	6.17
Means	8.91	6.38	9.20	8.17	5.14	6.90	5.37	6.47	5.84	4.96	6.12	5.23	7.43	4.62	6.96
S.D.	4.89	3.92	5.54	4.66	4.19	4.88	3.08	3.62	4.02	3.08	3.92	3.06	3.35	3.12	2.86

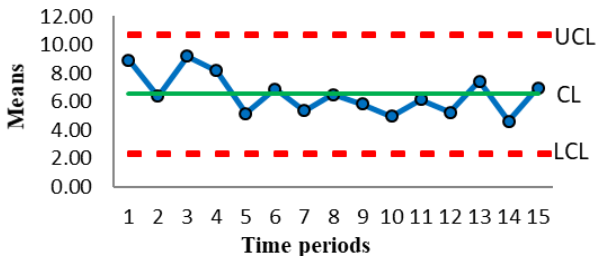

Figure 1. Mean chart of MS causing cells.

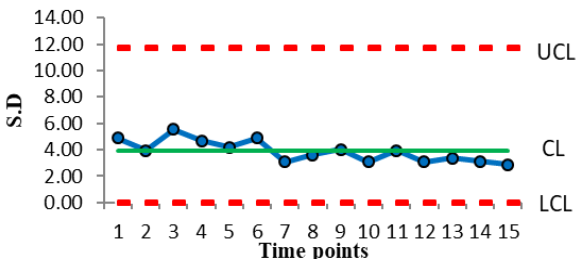

Figure 2. Control limits of s chart for MS causing cells.

To conduct a similar analysis for oligodendrocytes, the average sizes of oligodendrocytes were computed and are shown in Table 3. The mean values of oligodendrocytes at various time points are 3.91, 5.14, 7.14, 4.97, 6.01, 4.6, 5.29, 7.14, 5.51, 6.67, 4.81, 4.72, 7.34, 6 and 6.93. Sample size (n)=8; overall mean $E(\bar{Y})$=5.74; overall standard deviation S.D(Y)=2.07; and control limits of mean chart are $E(\bar{Y}) \pm 3S.E(\bar{Y})$. Here, the Upper Control Limit $\left(UCL_{\bar{y}}\right)$ is 7.94; the Lower Control Limit $\left(LCL_{\bar{y}}\right)$ is 3.55; and the Central Limit $\left(CL_{\bar{y}}\right)$ is 5.74. The control chart for mean of oligodendrocytes is constructed using the above observations. In Figure 3, it is observed that standard sizes of oligodendrocytes are

Table 3. The expected number of oligodendrocytes $E(b_i)$ at different time periods.

λ_{2i}	μ_{2i}	t	$E(b_i)$	λ_{2i}	μ_{2i}	t	$E(b_i)$	λ_{2i}	μ_{2i}	t	$E(b_i)$	λ_{2i}	μ_{2i}	t	$E(b_i)$	λ_{2i}	μ_{2i}	t	$E(b_i)$
2.5	1.2	1	5.1	1.6	1.7	2	1.2	2.3	1.8	3	6.5	2.3	1.9	4	5.9	2.5	2.1	5	7.3
2.5	1.3	1	4.5	2.4	1.5	2	7.7	2.3	1.8	3	7.1	2.2	1.9	4	4.8	2.5	2.2	5	5.4
2.4	1.2	1	4.9	2.2	1.6	2	5.0	2.3	1.8	3	5.9	2.1	1.9	4	3.7	2.6	2.6	5	1.3
2.6	1.2	1	5.7	2.4	1.7	2	6.0	2.3	1.7	3	9.0	2.6	2.1	4	8.5	2.6	2.3	5	6.9
2.5	2.6	1	1.4	2.5	1.6	2	8.5	2.3	1.7	3	7.7	2.4	2.0	4	6.9	2.5	2.2	5	7.3
2.6	1.9	1	3.0	2.0	1.6	2	3.1	2.3	1.8	3	5.6	2.4	2.4	4	1.4	2.6	2.3	5	7.7
2.7	2.0	1	2.8	2.0	1.6	2	2.9	2.4	1.8	3	8.5	2.4	2.1	4	4.0	2.6	2.2	5	8.1
2.6	1.6	1	3.8	2.5	1.7	2	6.8	2.2	1.6	3	6.9	2.6	2.3	4	4.7	2.4	2.2	5	4.2
1.6	1.3	6	5.9	2.3	2.1	7	6.5	3.1	2.9	8	8.8	1.6	1.4	9	7.1	2.7	2.5	10	6.9
1.4	1.3	6	3.7	2.4	2.1	7	8.6	2.8	2.6	8	6.9	1.8	1.6	9	7.7	2.7	2.5	10	8.5
1.4	1.3	6	3.7	2.4	2.2	7	4.0	3.5	3.3	8	8.1	1.9	1.8	9	4.1	2.5	2.3	10	6.3
2.0	1.7	6	6.3	2.4	2.2	7	5.7	3.5	3.3	8	7.5	1.8	1.7	9	5.9	2.5	2.3	10	5.1
2.0	1.7	6	7.5	2.5	2.3	7	5.3	3.5	3.3	8	5.5	2.0	2.0	9	1.3	2.6	2.5	10	8.5
1.9	1.7	6	4.7	2.4	2.2	7	7.0	3.6	3.4	8	8.1	1.9	1.7	9	5.9	2.6	2.4	10	6.9
1.9	2.0	6	1.2	2.3	2.2	7	4.0	3.5	3.4	8	4.7	1.9	1.8	9	4.9	2.6	2.5	10	3.4
1.9	1.7	6	3.9	2.5	2.5	7	1.1	3.6	3.4	8	7.5	2.1	1.9	9	7.1	2.8	2.6	10	7.7
3.2	3.1	11	3.4	3.3	3.2	12	3.2	3.0	2.9	13	7.6	2.7	2.7	14	1.2	2.5	2.4	15	7.3
3.1	3.0	11	7.3	3.3	3.2	12	4.7	3.1	3.0	13	8.6	2.9	2.7	14	6.5	2.4	2.3	15	6.3
3.2	3.2	11	1.1	3.3	3.2	12	7.5	2.9	2.8	13	5.9	2.8	2.7	14	5.7	2.6	2.5	15	6.3
3.4	3.2	11	8.1	3.4	3.3	12	5.2	2.9	2.8	13	6.7	2.8	2.7	14	7.5	2.6	2.5	15	7.3
3.3	3.2	11	3.0	3.4	3.3	12	6.7	2.8	2.7	13	5.1	2.8	2.7	14	6.5	2.6	2.5	15	7.3
3.4	3.2	11	6.5	3.2	3.1	12	3.2	2.8	2.7	13	8.6	2.9	2.8	14	6.5	2.6	2.5	15	6.3
3.1	3.0	11	4.2	3.1	3.0	12	2.6	2.9	2.7	13	7.6	2.7	2.6	14	7.5	2.5	2.3	15	8.5
3.2	3.1	11	4.7	3.4	3.3	12	4.7	2.9	2.8	13	8.6	2.7	2.6	14	6.5	2.5	2.4	15	6.3

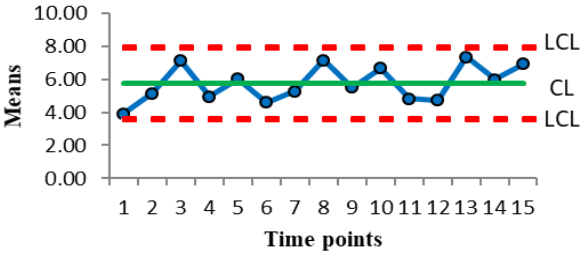

Figure 3. Mean chart of oligodendrocytes.

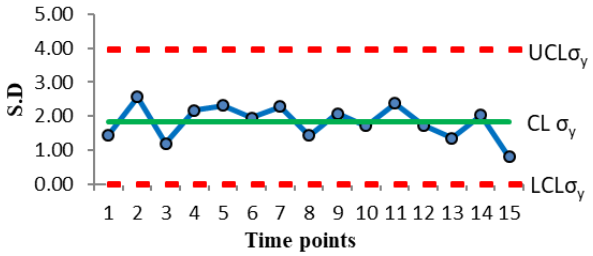

Figure 4. s chart for oligodendrocytes.

meeting the natural tolerance so that the standard of process is under control.

Extended data regarding the volatility of oligo-dendrocytes is presented in Table 4. The control limits for the variability of sizes in oligodendrocytes are computed with the notion of process capability or natural tolerance. The calculated standard deviations at various time points are 1.44, 2.57, 1.2, 2.17, 2.3, 1.95, 2.28, 1.42, 2.08, 1.71, 2.37, 1.73, 1.35, 2.02 and 0.8; The sample size n=8; $E(s)=1.83$ and $V(s)=4.28$. Therefore 's' chart limits are 1.83±4.28(0.5); the upper control limit of S.D ($UCL_{\sigma y}$) =3.97; the lower control limit of S.D ($LCL\sigma_y$) =-0.31, since $\sigma_y \geq 0$, then $LCL\sigma_y$ =0, Central Line ($CL\sigma_y$) =1.83. The above results were used to construct the control chart for standard deviation of oligodendrocytes, shown in Figure 4. It is observed that standard deviation of number of oligodendrocytes is under control, indicating that the volatility of oligodendrocytes is under control.

4. Conclusions

Development of healthcare devices through statistical quality control for optimal health management of MS disease was the core objective of this study. The control limits were constructed based on the derived statistical relations. The devices, namely UCL and LCL, were computed based on sampling distributions from simulations. Hypothetical data were considered for studying the status of the quality assurance through Mean and Standard Deviations. The control limits for assessment of quality standards were fixed with UCL and LCL. The analysis was carried out with control limits where natural tolerance or 3σ limits are considered. Quality devices were derived through the control limits for both standard and volatility measures. Variances of MS causing cells and oligodendrocytes will provide the allowable and observed fluctuations on the health variations. These will provide the measures of volatility in health standards.

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Table 4. Final results of the expected number of oligodendrocytes.

S. No.	t_1=1	t_2=2	t_3=3	t_4=4	t_5=5	t_6=6	t_7=7	t_8=8	t_9=9	t_{10}=10	t_{11}=11	t_{12}=12	t_{13}=13	t_{14}=14	t_{15}=15
1	5.14	1.15	6.47	5.91	7.29	5.91	6.53	8.82	7.07	6.93	3.38	3.24	7.59	1.22	7.29
2	4.51	7.66	7.07	4.84	5.40	3.66	8.64	6.93	7.74	8.47	7.29	4.65	8.64	6.53	6.27
3	4.89	5.04	5.91	3.66	1.27	3.66	4.00	8.14	4.12	6.27	1.12	7.51	5.85	5.68	6.27
4	5.73	6.03	8.99	8.47	6.93	6.27	5.68	7.51	5.91	5.14	8.14	5.24	6.66	7.51	7.29
5	1.37	8.47	7.74	6.93	7.29	7.51	5.29	5.46	1.28	8.47	3.02	6.66	5.14	6.53	7.29
6	3.02	3.05	5.57	1.35	7.66	4.65	7.00	8.14	5.91	6.93	6.53	3.24	8.64	6.53	6.27
7	2.82	2.93	8.47	3.96	8.06	1.24	4.00	4.65	4.94	3.44	4.21	2.55	7.59	7.51	8.47
8	3.77	6.80	6.87	4.65	4.21	3.88	1.14	7.51	7.07	7.66	4.70	4.65	8.64	6.53	6.27
Means	3.91	5.14	7.14	4.97	6.01	4.60	5.29	7.14	5.51	6.67	4.81	4.72	7.34	6.00	6.93
S.D	1.44	2.57	1.20	2.17	2.30	1.95	2.28	1.42	2.08	1.71	2.37	1.73	1.35	2.02	0.80

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