Maximizing Efficiency of Amyloid Disease Subtyping by Tandem Mass Spectrometry: A Value Stream Approach

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Background

Mayo Clinic is the only institution in the world using shotgun proteomics to subtype amyloid disease; efficiency must be improved to accommodate increasing demand. We used DMAIC and value stream approaches to identify areas of waste and quality improvement. Focusing on instrument time, we determined that by upgrading our liquid chromatography system, we improve our patient analysis time by 2.5 hours/patient or ~30%. An analysis of technician time revealed that by reducing samples processed from 4 to 3, we would save 1 hour per patient. This project clarified the process workflow and uncovered quality improvement opportunities with large efficiency benefits.

Background

Amyloid disease is characterized by deposition of plaque-forming fibrils in most tissues of the body. Of diagnostic importance is the fact that amyloid plaques stain with Congo Red and fluoresce, making them easy to identify but not necessarily easy to characterize; prognosis and treatment are improved dramatically if the amyloid subtype is known. The immunostains development team, including Julie Vrana, Jeff Gamez and Jason Theis, in collaboration with the Mayo Proteomics Research Core, developed a test that could identify amyloid subtype from a Congo Red positive plaque dissected under magnified fluorescence and analyzed using shotgun proteomics. By its nature, the shotgun proteomics approach is complex and time consuming; to help the Mass Spec team, and those who are not familiar with our process, we sought to map the process and identify waste.

Objectives

Our primary goal in embarking on this adventure was to make our process more transparent. The higher the complexity of the process the more "black-box" it appears to outsiders. Secondary objectives were to organize our process into sections and identify at least one major process improvement opportunity in each. As our volumes continue to increase, and instrument capacity becomes tight, we recognize that it is time to evaluate efficiency.

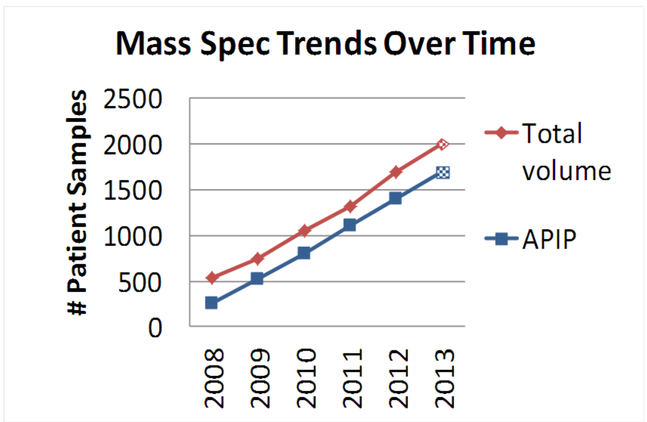

Figure 1: **Patient trends for 2012. (**Blue) Trends for paraffin samples track well with total volume (Red) which include development and non-dissected samples. A projection for 2013 is shown (current total volume for 2013 is 1605 patients).

Method

We used DMAIC and Value Stream Approaches to map the process and to identify opportunities for improved efficiency. Our process was split into three sections: **tech time**, **instrument time** and **lead time**, or turn around time.

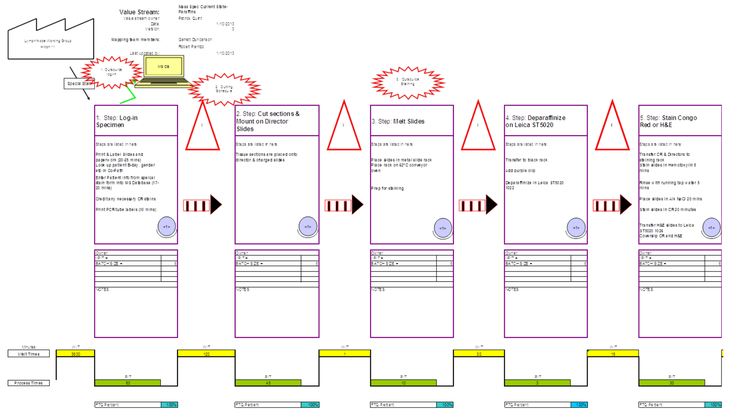

Figure 2: **A portion of our Value stream map used for determining opportunities for efficiency improvement**.

Results: Tech time analysis

Tech Time breakdown: Analyzing a breakdown of technologist time revealed that the largest portion of a technologist's time is spent dissecting. The process requires that an extra contingency (S4) sample be dissected, but in 2012 S4 was used only 1.96% of the time (25/1274 patients) Removing S4 from the process would save 10% or 32 full days over the course of a year.

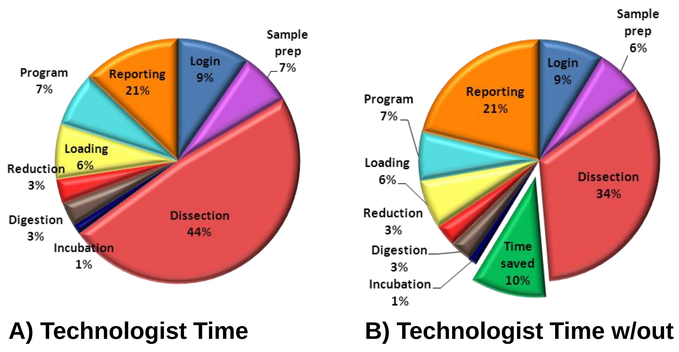

Figure 3: **Technologist time breakdown by percent effort.** A) The bulk of the technologist's time is spent dissecting Congo Red positive tissues including an extra contingency sample, S4. B) 10% time could be saved if, given the rarity of needing an S4, we decided it would be useful to remove it from the process .

Removing S4 dramatically improves efficiency: A pilot study removing S4 from the process, decreased the time required to dissect a single patient by ~15 minutes and ~1.5 hours/6 patient batch. This meant that more batches could be completed in 1 day and a 3 day improvement in average turn around time (TAT). If an S4 is required, it is easily, and quickly (15 minutes), dissected with the next batch.

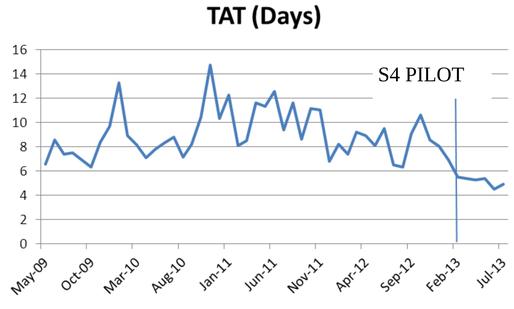

Figure 4: **Turnaround time is improved by removing S4**. Our turnaround time fluctuated dramatically when the test was first instated, then leveld off around 8 days in late 2011. Removing S4 meant more patients completed in 5 days.

Results: Instrument Time Analysis

Instrument Time Breakdown: We have two instruments in clinical use: the LTQ-Velos and LTQ-Orbitrap. Analysis of acquisition time on both revealed that the LTQ-Velos required ~30 more minutes to load a sample, meaning 1.5 fewer patients /day compared to the LTQ-Orbitrap. Additionally, instrument down time was significantly higher for the LTQ-Velos (11.4% DT compared to ~3.5% DT for the LTQ-Orbitrap). By installing a pump similar to that on the LTQ-Orbitrap, we projected a 31% increase in open capacity and a decrease of 8% total in unplanned maintenance.

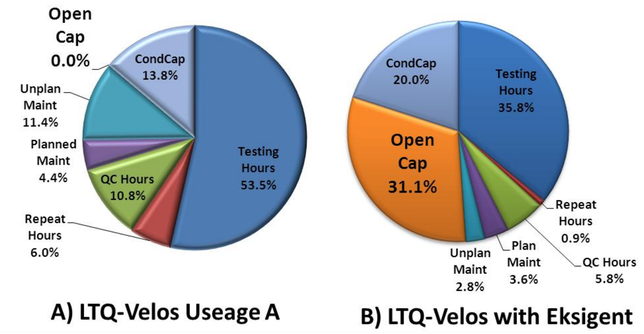

Figure 5: **Installation of an Eksigent nano 2D LC increases capacity.** A) A usage chart for the LTQ-Velos indicates high percentages for testing hours and unplanned maintenance compared to B) the same instrument with an Eksigent pump installed.

Eksigent installation improves capacity: Following installation of the Eksigent pump, patient volumes/day increased from 2.9 patients/day to 4.5 patients/day and improved the instrument capacity (Figure 6). This improvement also contributed to TAT improvement (Figure 4).

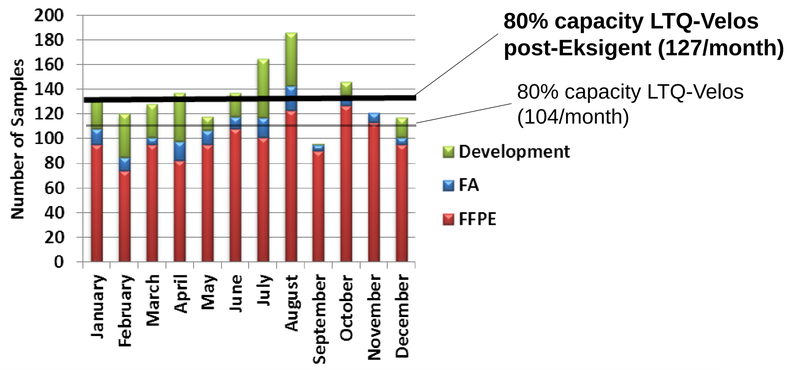

Figure 6: **80% instrument capacity was improved by installing the Eksigent pump**. A standard 20% conditional capacity allows for down time and maintenance. With the addition of the new pump, we went from cutting deeply into our conditional capacity to nearly meeting it in 2012 (retrospectively). Delopment and Fat Aspirate (FA) are additional samples that are not factored into the estimates in this project.

Results: Turn Around Time

In addition to the TAT improvements achieved by removing S4 and installing the Eksigent pump, we are working on a digestion method that will reduce the process by 24 hours. Early data suggest a data improvement benefit as well.

Conclusions

- Relatively minor changes equated to major time savings
- Standardization of equipment improved TAT and quality of data
- Quality tracking programs in place were essential in demonstrating feasibility of proposed changes.