Workflow Whitepaper

Patient Case Management Improves Workflow in IHC Labs

Agilent Dako

Introduction

Immunohistochemistry (IHC) is a central method in the diagnosis of cancer. The visual detection of biomarkers by IHC helps pathologists classify cancer, which is crucial for identifying the best possible treatment for each patient. Cancer prevalence is increasing[1] and the number of new biomarkers for cancer classification is also growing[2]. Despite the increased testing requirements, many labs doing IHC staining are not seeing corresponding budget increases.

IHC Workflow Processes

There are two main 'schools' of IHC workflow processes: Large batching or continuous loading in smaller batches. It is a common belief that a larger batch size translates to higher productivity or that efficiency, and therefore higher productivity, can only be achieved with more platforms. However, an important factor in improving productivity is achieving an optimal transfer of workload and shorter cycle times that will make the process run more smoothly.

A workflow that involves continuous loading of slides in smaller batches more regularly creates a snowball effect of smaller batches being ready sooner, delivered earlier and reviewed more quickly.

The various staff in of an IHC lab have different priorities for the workflow. A workflow improvement that benefits all stakeholders should, among other things, reduce hands-on time for the technicians, increase the throughput for the lab managers and provide quicker results for the complete patient case to the pathologists.

Team members' top priorities in IHC workflow

Technicians	Lab Managers	Pathologists
– Hands-on time – Ease-of-use	– Throughput – Capacity	– Time to result – Quality – Complete cases

Figure 1. IHC lab staff have different priorities. The end goal is to have complete patient cases ready for assessment by the pathologist earlier.

Definition of Patient Case Management

The process of keeping slides belonging to the same patient case together throughout the workflow as much as possible, including keeping the slides in the same rack on the same instrument, regardless of the primary antibodies or detection system used.

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Patient Case Management

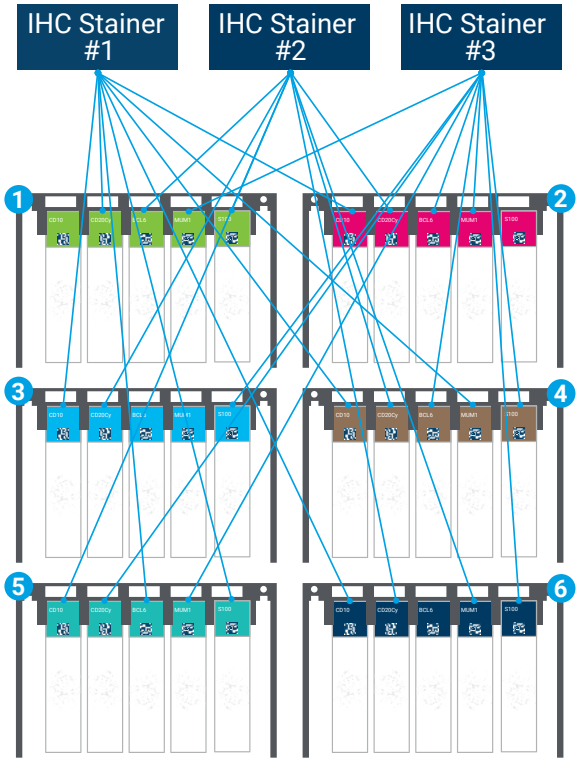
Patient Case Management (PCM) utilizes the effect of loading continuously in smaller batches, i.e. the patient case is defined as one small batch. The PCM workflow process is centered around each individual patient case, where the goal is to keep slides belonging to the same case together in the whole process. The patient centric 'togetherness' of slides for the same patient case applies to both space and time meaning that a case should be considered an entity that is stained together - in the same timeframe - to allow a continuous flow of complete patient cases to the pathologists for a diagnostic decision.

The fundamental principle behind PCM is working in a LEAN manner, where the final product is kept as a unit during the process. In this case, the product is the entire patient case (not the individual slides) and with the suggested tactics below, it is possible to reduce sorting of slides both before loading the slides and after staining. These sorting steps are not only complex and time consuming, but staining slides belonging to the same case on different instruments will also delay the completion of the case, because slides in split cases are not started at the same time on the different instruments.

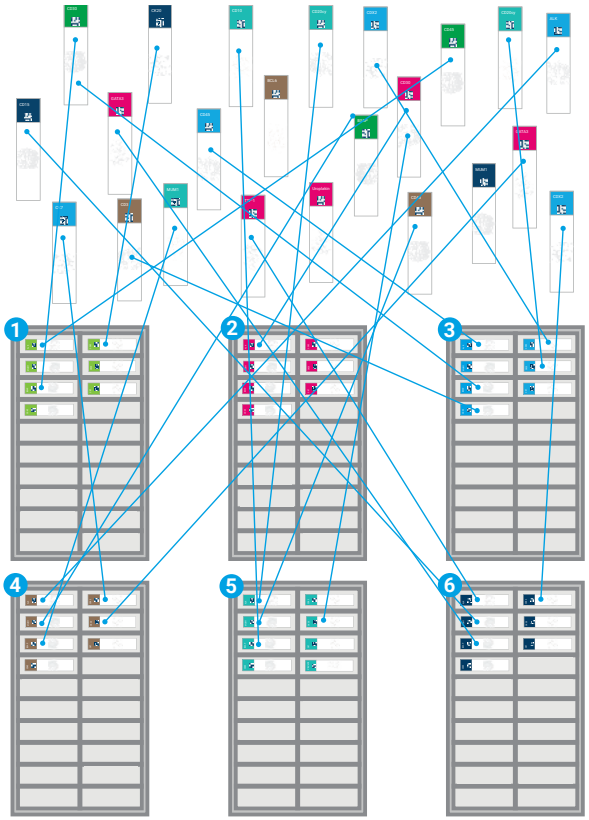
To implement a PCM workflow in an IHC lab, several main processes must be in place:

- Process cases on demand - continuously
- First in -> first out
- Load slides by case, not by antibody
- Minimize splitting of cases on different instruments
- Minimize re-assembly after staining by keeping the cases together
- Distribute complete patient cases to pathologists throughout the day

Batch Mode: six patient cases split on three IHC stainers



A) Slide sorting in large batch mode.: The patient cases are organized by primary antibody. The batches of slides per antibody are then organized and loaded per instrument where the needed antibodies are located, resulting in patient cases being shuffled across multiple instruments.



B) Post-staining re-assembly of cases in large batch mode: After staining, the split cases have to be re-assembled into their respective case folders that contain the H&E stains and maybe Special Stains for that patient case.

Figure 2. IHC slides belonging to six patient cases are split onto three different instruments depending on where the primary antibody for each slide is located. This causes both pre- and poststaining sorting.

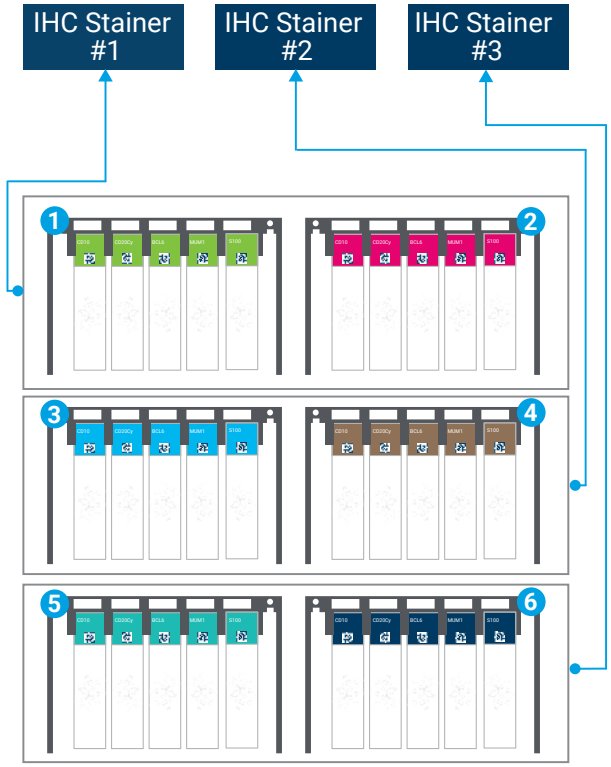
In a small volume pathology lab using a limited number of different antibodies, it is usually easy to load each patient case and the reagents needed on one instrument and keep the slides in the same rack. However the challenges begin when there are many patient cases waiting to be stained with many different antibodies.

Figure 2 shows a simple example of what happens when there are slides for six patient cases waiting to be stained on three instruments. In this example, the individual instruments have limited reagent positions for all the antibodies and all the visualization system vials, so slides belonging to the same case must be split according to the instrument that carries the antibody required for the individual slides. This pre-staining sorting and post-staining re-assembly of cases is time-consuming in terms of hands-on time. And more importantly for time to diagnosis, slides stained on different instruments in different racks are not completed at the same time, which will delay the re-assembly of the complete patient case.

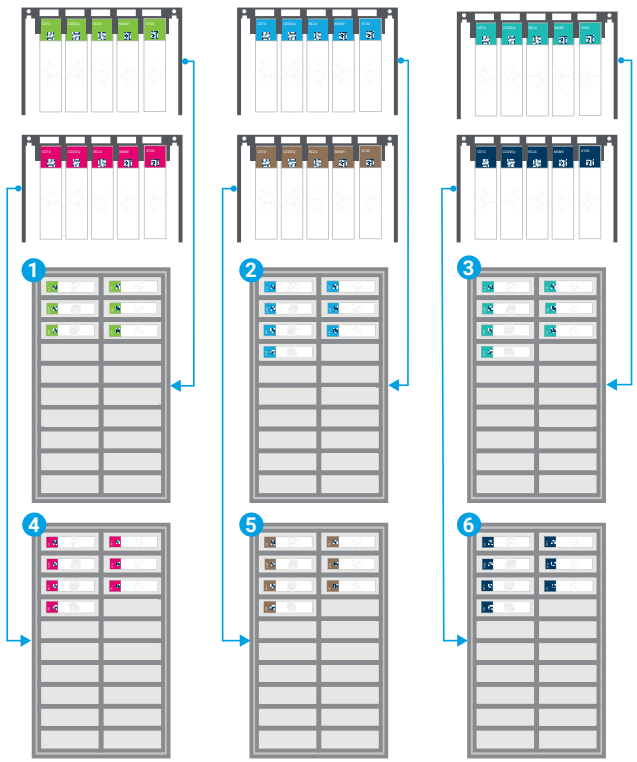
In a PCM workflow, this splitting is prevented as much as possible. Slides for a patient case are kept in the same rack and stained on the same instrument. This puts some challenges on the available equipment, which has to support a large reagent capacity and support continuous loading of cases so a first in -> first out process can be obtained.

Having a large reagent capacity means that the primary antibodies can be loaded onto a free instrument whenever a patient case is ready to be stained. For some of the most frequently used antibodies, a duplicate antibody vial may be needed so two different cases requiring the same antibodies can be run simultaneously on two different instruments. In figure 3, a schematic illustration shows how the same six patient cases are run in a PCM workflow. By loading the slides in the same rack together with antibodies and visualization system for each patient case on the same instrument the pre- and post-staining sorting is eliminated. And since the stained slides are completed at the same time, the complete patient case can be delivered directly to the pathologist for assessment.

PCM Mode: Six patient cases stained on three instruments.



A) Slides belonging to the same cases are kept in the same rack and stained on the same instrument. The reagents for each case are loaded onto the instrument at the same time.



B) The six cases have been stained and reassembly into complete patient cases is easier as the slides belonging to the same cases are stained in the same rack on the same instrument whenever possible.

Figure 3. PCM workflow: Whenever possible, all slides for a case are loaded in the same rack and stained on the same instrument loaded with the required reagents for the slides in the rack. This reduces hands-on time and ensures that slides belonging to the same case are completed at the same time for delivery to pathologists.

The impact upon productivity by the two different workflow approaches (large batches versus PCM) was analyzed in two pathology laboratories. The labs were analyzed before and after implementation of new equipment that facilitates continuous loading and has a large reagent capacity to hold antibodies and reagents for the PCM workflow model.

Study Design

Site 1[3]: In the 'before' workflow study in 2016, hands-on time was recorded for a subset of 49 cases, i.e. 28 cases with 144 slides on their former platforms. In the "after" workflow study with Dako Omnis installation in 2017, hands-on time was recorded for a subset of 37 cases, i.e. 27 cases with 131 slides. The measured parameters were: hands-on time (cutting, mounting, sorting, loading slides, preparing reagents and loading/unloading reagents, unloading slides and re-rack, washing slides, dehydrating, coverslipping, unloading, sorting, QC, sign out) as well as delivery times.

Site 2[4]: The first analysis in 2017 mapped out their old workflow system with five of their former stainers, measuring 85 cases with 308 slides over 3 days. After installation of two Dako Omnis platforms and new processes including PCM workflow had been successfully implemented, another workflow analysis was conducted. Over a period of 3 days analyzing the new Dako Omnis setup, 108 patient cases using 442 slides were timed. The measured parameters were: hands-on time (preparing and loading reagents, prepare dilution, sorting, QC) and continuous delivery of cases.

Results

Hands-on time

The first measurement of improved workflow is hands-on time. The less time staff use on practical tasks such as slide sorting, reagent preparation, washing, etc., the more time they can spend processing cases.

In the two sites, each practical task that each lab technician performed was measured on a stopwatch by the two Agilent Workflow Team observers. The measured times were recorded and an average of hands-on time per slide was calculated.

For Site 1, the 37% reduction in hands-on time was mainly driven by more efficient pre- and post-staining sorting, accounting for 71% of the total reduction. At Site 2, a 36% reduction in hands-on time was achieved of which, the reduced time spent on pre- and post-staining sorting accounted for 36% of the total hands-on time reduction. The difference is attributed to cutting and mounting times being included in Site 1, but not in Site 2.

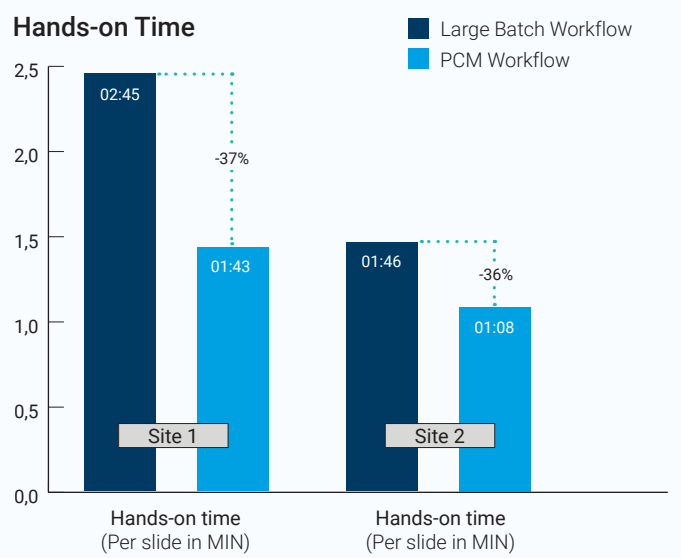


Figure 4. Site 1 was calculated as an average per slide based on measurements of n=144 and n=131 slides, before and after, respectively. Site 2 hands-on time was calculated based on measurements of n=80 and n=87 slides, before and after, respectively. Note that for Site 1, hands-on times for cutting and mounting are included, but not for Site 2 data.

Turnaround time

Turnaround time is often defined as the time it takes for a slide to be stained. However, from a patient case perspective it is more relevant to define turnaround time as the time from request to delivery of the full patient case back to the requesting pathologist. What good is a single slide's staining time when all of the patient case's slides need to be ready before the pathologist can make a diagnosis? In a PCM-based workflow, a reduction in time to delivery of complete patient cases is an overall goal.

In Site 1, this goal was represented by the number of cases the lab was able to deliver back to the pathologists the same day the tests were requested. Converting from a batch workflow to a PCM workflow enabled the lab to complete a higher number of full patient cases on the same day as the test request was submitted.

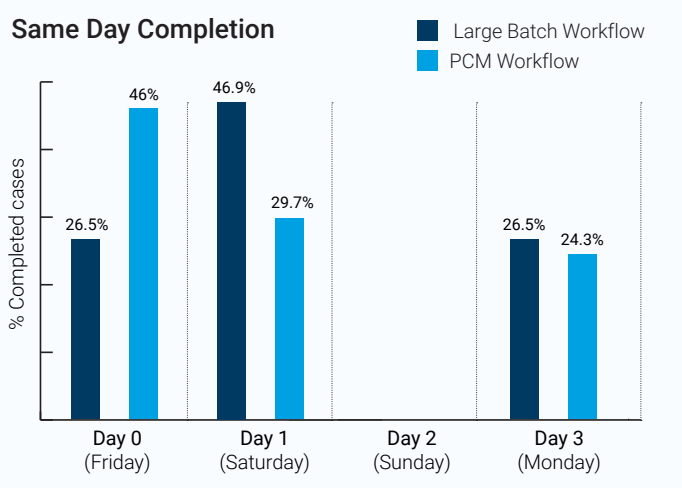


Figure 5. Site 1. Completion of cases on the same day as requested was increased after implementing PCM workflow.

The lab managed to complete 26.5% of cases using the large batching workflow, but switching to a PCM workflow on Dako Omnis increased the percentage of cases that were completed the same day as requested to 46%, up by 74%.

At Site 2, cases completed on the same day were delivered 40 minutes faster (12% decrease) in the PCM workflow setup. Patient cases that included an overnight run were finalized more than 2 hours sooner (10% decrease) in the new PCM workflow compared to the old workflow.

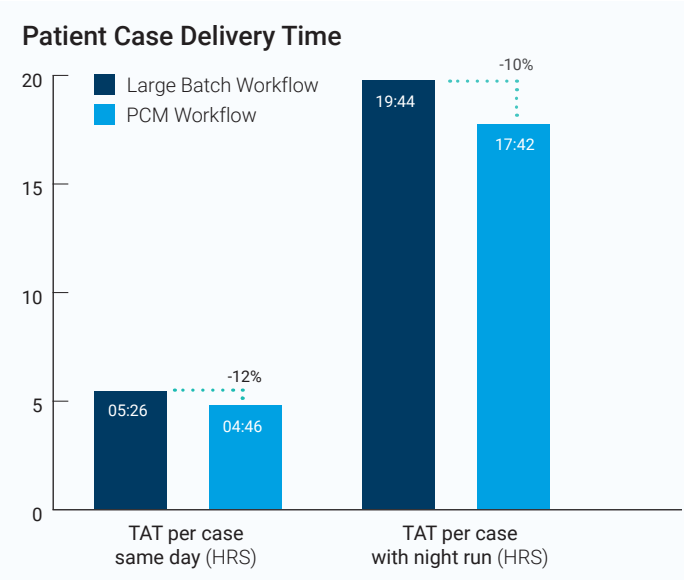


Figure 6. Site 2 comparison of turnaround time before and after installation of two Dako Omnis solutions. Number of slides before and after = 80 and 87, respectively. Number of cases before and after = 19 and 15, respectively. Only cases that were started Day 1 and completed on Day 1 are included in 'TAT per case same day'. Only cases that were started Day 1 and completed on Day 2 are included in 'TAT per case with night run'.

Continuous delivery of patient cases

Sorting of slides that are finished in big piles once or twice per day is one of the reasons for the documented higher hands-on time used in large batching mode. Here, slides have to wait for other slides in the same case to be completed, thus increasing re-assembly time and causing a big batch to be delivered at the end of the day.

When slides belonging to the same case are delivered continuously in small batches as complete patient cases throughout the day, it becomes easier to manage each case and ensure a faster and more evenly distributed delivery of cases to the pathologist.

At Site 2, we compared how slides were delivered before and after implementation of PCM workflow.

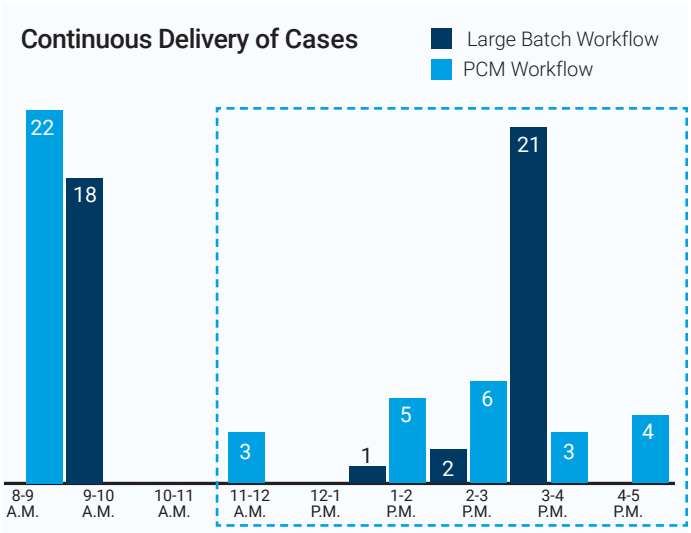


Figure 7. Before the Dako Omnis upgrade, slides were delivered in a big batch in the afternoon. With Dako Omnis, cases are completed continuously throughout the day (highlighted area). Overnigth runs are delivered in the morning.

It is clear that using the PCM workflow model on Dako Omnis ensured that cases were delivered in small, steady numbers throughout the afternoon instead of in one big batch in the afternoon (3-4 p.m.). By continuous loading and unloading throughout the day, the delivery of complete patient cases to pathologists is faster, smoother, and less stressful.

Capacity

PCM workflow enables laboratories to process more slides, and thus more patient cases, per day. Results from labs implementing a PCM workflow on Dako Omnis have shown that:

- **Site 1**: This lab changed their four old stainers to two Dako Omnis platforms and were able to increase the number of patient cases completed within the same day as the requests were received by 74%.
- **Site 2:** This lab changed their five old stainers to two Dako Omnis platforms and were processing 8% more slides on the Dako Omnis platforms. And they also added ISH slides to their staining services.

Table 1. Fewer platforms used in a PCM workflow can increase capacity.

		Before	After	Change
Instruments				
	Site 1	4 instruments	2 Dako Omnis	-50%
	Site 2	5 instruments	2 Dako Omnis	-60%
Capacity (year)				
	Site 1	22,000 slides	25,000 slides	+12%
	Site 2	44,587 slides	48,284 slides	+8% (+ISH)

Conclusions

When the two labs switched to Dako Omnis and fully implemented the patient case management workflow mode, they experienced a reduction in hands-on time and were able to complete more patient cases within the same day as the requests were received and deliver cases continuously throughout the day.

Benefits from Dako Omnis and patient case management workflow:

- Reduced need to divide patient cases between multiple instruments
- Reduced hands-on time by 37% and 36%, respectively in two laboratories
- Reduced need for slide sorting before and after a run
- Increased number of patient cases finalized the same day by 74% (Site 1)
- Patient case completion time reduced by 12% (Site 2)
- Capacity increased by 8% and 12% at Site 1 and 2, respectively

Acknowledgment

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