

Automating the cytogenetics process

Automation has brought about many benefits at the cytogenetics laboratory of an Italian regional hospital

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The cytogenetics laboratory at the Regional Hospital of Treviso performs tests in different fields of clinical medicine including cancer cytogenetics (onco-haematology and solid tumours) and postnatal tests to detect constitutional abnormalities. The laboratory analyses approximately 2200 cases per year.

Techniques employed and clinical indications

The main techniques employed are: karyotyping/chromosome analysis; fluorescence *in situ* hybridisation (FISH); and comparative genomic hybridisation (array-CGH).

Karyotyping

Classical cytogenetic analysis is carried out on peripheral blood, skin and bone marrow samples to detect constitutional and acquired abnormalities. The clinical indications for investigation of constitutional karyotype are:

- Primary or secondary amenorrhoea or premature menopause
- Sperm abnormalities, such as azoospermia or severe oligospermia
- Clinically significant abnormal growth



“Automation has boosted the quality of our service for the good of the patients”

- Ambiguous genitalia
- Abnormal clinical phenotype or dysmorphism
- Multiple congenital abnormalities
- Intellectual disability or developmental delay;
- Suspected deletion/duplication syndrome
- A malformed foetus or stillbirth of

unknown aetiology

- Third and subsequent consecutive miscarriages.
Couples with:
- Chromosome abnormality or unusual variant detected at prenatal diagnosis
- Unbalanced chromosome abnormality in the products of conception
- Child with a chromosome abnormality
- Infertility of unknown aetiology.

The clinical indications for investigation of acquired karyotype include: acute leukaemia; myelodysplasia; chronic myelogenous leukaemia; chronic myeloproliferative neoplasms; malignant lymphoma and lymphoproliferative disorders; and chronic lymphocytic leukaemia.

Side volume for karyotyping is 850 cases/year.

FISH

FISH is employed on cytological samples (peripheral blood and bone marrow) and histological sections of solid tumours. Side volume for FISH is 1200 cases/year.

Array-CGH

Carried out on DNA extracted from blood samples and histological sections.

Clinical indications include:

- Clinically significant abnormal growth
- Abnormal clinical phenotype or dysmorphism
- Multiple congenital abnormalities



- Intellectual disability or developmental delay
 - Suspected microdeletion / microduplication syndrome
 - Brain tumours.
- Side volume for this technique is 150 cases/year.

Moving to an automated cytogenetics platform

The aim had always been to automate the cytogenetics process from the sample preparation step to the analysis, because we believe that automation is key to improving standardisation methods and to the accuracy and quality of analysis, increasing efficiency, reducing turnaround times, avoiding operator variability (a critical point in cytogenetic services) and ultimately strongly boosting the quality of our service for the benefit of the patients.

The first automatic instrument (a platform for scanning and capturing metaphases) was acquired through a

donation from the Italian Leukaemia Association. The resultant increased output without the requirement for increased numbers of personnel led us to purchase other automatic platforms.

Selecting CytoVision

I had previously used the CytoVision software (Leica Biosystems) while training at the cytogenetic laboratory of the Hospital Clinic in Barcelona and was impressed by its ease of use and multiple, useful features. The platform offers the convenience of on-screen analysis with flexibility of both software and hardware configurations. The software interface is user-friendly and easy to use, and generates excellent image quality.

In Treviso, we first started with a semiautomatic microscope, and year-by-year, gradually implemented the automation process. CytoVision was fully introduced into our routine practice in 2003 and all karyotyping and FISH tests now being performed with the

CytoVision platform.

Implementation

Implementation was easy; even more so when we introduced the GSL-120 system (Leica Biosystems) instead of the multi-bay stage. The GSL-120 system is a platform for brightfield and fluorescent samples, which processes up to 120 slides per batch and automatically feeds these onto the scanning stage. The multi-bay stage is eight slides, so requires more user interaction to swap out slides. Using the GSL-120 had a considerable impact on reducing the reporting time and we now have one GSL-120 for every four users.

User experience

Key benefits experienced include:

- Ease of training and ease of use
- Easy adoption: users were easily accustomed to the new system and were pleased to move to it.
- Image quality is consistently excellent, leading to fast and accurate processing and reduced turnaround time
- Onscreen analysis for FISH reduces the time spent in the darkroom
- Can scan and capture a high number of metaphases in those samples that have few abnormal metaphases (Figure 1).

Cost savings

With automation, we save around 40 minutes per case (57% reduction) to search for and capture 30 metaphases. A 57% cost saving translates to €19 for each case of 30 metaphases. So, with 850 karyotyping cases per year, this could equate to a potential saving of €16,150 per annum.

Conclusions

Automation has brought about many benefits over manual processing, not only for our personnel but also in terms of patient management. It has impacted speed of reporting and has maximised efficiency of our laboratory. Automation has ultimately boosted the quality of our service for the good of the patients and, in the future, it is likely that automation will enable us to enhance our facility's tests menu thereby allowing us to serve an even wider range of patients. ♦

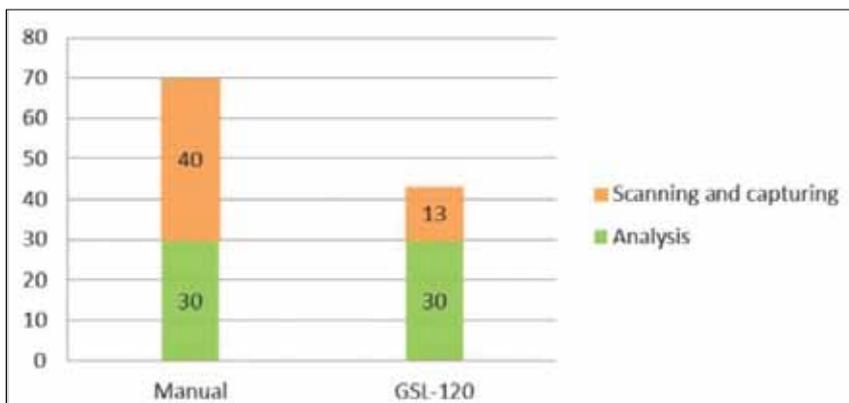


Fig 1: Time to search, capture and analyse 30 metaphases