Tissue archiving: reality, recommendations, and best practices

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Institut national de la senté et de la recherche médicale



Learning Objectives

- Review tissue block archiving guidelines in the US and discuss how these regulations compare to those in other countries throughout Europe.
- Examine how one laboratory achieved time-savings while improving compliance with their tissue block archiving system.
- Identify best practices towards improving your laboratory's efficiency in tissue block archiving.

Paraffin blocks management: main challenges

Increased block volume:

- Cancer incidence
- Aging population
- Improvement of standards of care
- Legal retention period



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- Second opinion
- Research projects
- Clinical trials



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...with shortage of technicians and lab resources



Agenda

- Part 1: Paraffin blocks archiving: legal, recommendations and facts:
 - 1 identification
 - 2 conditions of storage and retention period
 - 3 retrieval tracking
 - 4 long-term archiving economical issue

• Part 2: Evaluation of a new block management system

Part 1: Paraffin blocks archiving: legacy, recommendations and facts

1-Identification!



Patient misidentification in laboratory medicine?

- 253 root cause analysis reports from the Veterans Health administration, collected between 2000 and 2008
- Patient misidentification: 182 adverse events (72%)
- Stage of the test cycle:
 - 132 misidentification events occurred in the pre-analytic phase and
 - Only 37 events (20%) occurred in the analytic phase: 4 failure for cancer diagnosis
 - 13 in the post-analytic phase
- Manual entry and limiting the patient identifier to accession number contributed to specimen misidentification

Study of mislabeling of cases, specimens, blocks and slides in 136 institutions

- Participants prospectively reviewed surgical pathology cases for 8 weeks and identified all mislabeling errors
- 1811 mislabeling occurrences:
 - 0,11% Cases: (490 of 427 255)
 - 0,1% Specimens (796 of 774 373)
 - 0,17% Blocks (2172 of 1 304 650)
 - 0,11% Slides (2509 of 2 261 811)
- In 96,7% of cases, errors were corrected before reports were issued
- In 1,3% of errors occurrences, participants gauged that patient care was affected

Arch Pathol Lab Med 2011;135:969-974

Study of mislabeling of cases, specimens, blocks and slides in 136 institutions

- 3 points in the process must be tightly controlled:
 - Accessioning
 - Transferring tissue into blocks
 - Tissue cutting and slide mounting
- The mislabeling rate was lower in institutions that :
 - Used automatic labelers integrated with accessioning systems
 - had a continuous (one by one)individual-case accessioning and processing (Avoid batch work)

CAP guidelines: blocks must have TWO identifiers

- The accession number:
 - A letter for Histology, Cytology or Autopsy
 - The year
 - LIS accession number
 - Example: 16H-9999-1-A
- Second identifier:
 - Barcode
 - Patient name or initials
 - Patient's birthday



• If possible, the anatomical site can also be added

Arch Pathol Lab Med . 2015;139(12):1515-24.

2- conditions of storage and retention period



Parmesan (parmigiano reggiano) cellar in Italy (35000 m2), owned by the Milanese bank: Credem, This cheese ensures the repayment of the loans of the producers

- Neither consent nor a license is required for the storage of material for diagnostic purposes for the benefit of the person from whom the tissue was removed during life.
- Pathology departments are responsible for the oversight and protection of this material



The facilities

- Legal dispositions of conservation of medical records:
 - stored specimens should remain intact and accessible for the full term of their retention
 - The facilities must be locked to ensure confidentiality of records
 - No alteration of temperature, humidity, no direct sun light
 - About 18°C (66°F) with humidity of about 50%
- Regarding paraffin blocks there are very few recommendations:
 - Temperature <26° (78°F) and > 30% and <70% humidity
- Proteins and DNA are quite stable over time but not RNA

Xie R, Chung JY, Ylaya K, et al.. *Factors influencing the degradation of archival formalin-fixed paraffin-embedded tissue sections.J Histochem Cytochem. 2011 Apr;59(4):356-65.*

Retention periods: 3 levels

 Law: Very few specific legal requirements in this field: usually between 2 to 10 years according to countries

 National college of pathologists: established some recommendations superior to legacy duration

 State or institution policies: at least equal to college recommendations

Paraffin block retention periods around the World

country	references	periods
USA	CLIA 88 Record Retention Requirements (42 CFR 493,1105)	2
	CAP guidelines (2016)	10
	New York State	20
	Duke University Health System laboratories (2016)	indefinite
Canada	Canadian Association of Pathologists	20
	Ontario laboratory guidelines	20
	Alberta Health service (2016)	30
Australia	Australian government Department of Health (2013)	10

Paraffin blocks retention periods around the World

country	references	periods
France	10	
	Public laboratories: Considered as part of medical records	20
Belgium	Code déontologie belge	30
Netherland	Netherland Dutch pathologist spciety	
Italy	Ministry of health (2016)	10
Germany Musterberufsordnung, MOB ×10 (1998)		12
United Kingdom Royal College of Pathologists (2015)		30
Switzerland (Geneva)	Cantonal laws	indefinitely

Retention periods: remarks

 Retention time for children is usually longer (until the child reached the age of 25). In most cases, to comply to these standards all paraffin blocks have to be retained for the extended period

 In case the initial diagnostic materials were discarded, patients are not eligible for enrollment in clinical trials

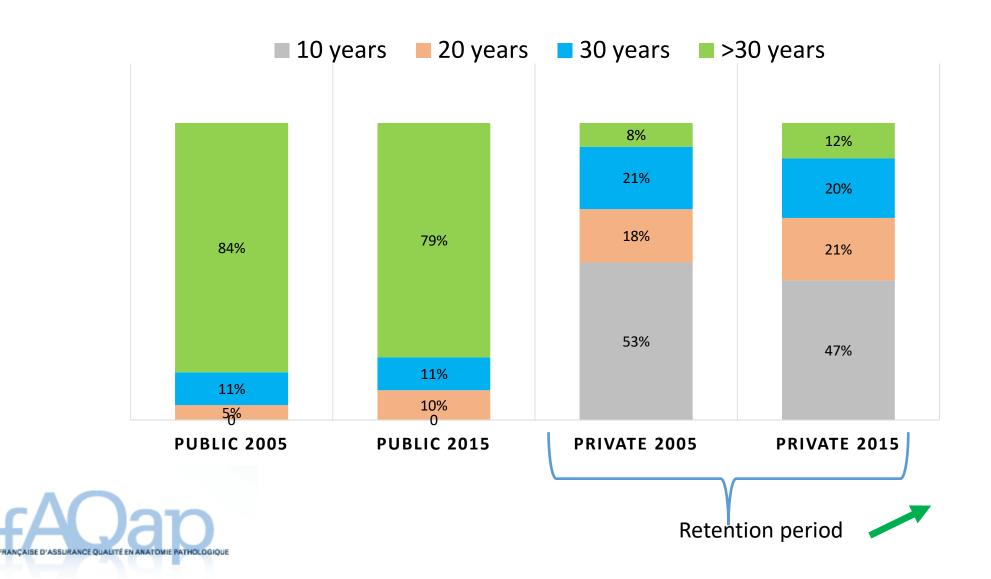
> Call for Revision of College of American Pathologists–Mandated Requirements for Retention of Laboratory Records and Materials

Department of Pathology

NICHOLAS J. VOGELZANG, MD Department of Hematology/ Oncology Nevada Cancer Institute Las Vegas, NV 89135

Arch Pathol Lab Med-Vol 132, November 2008

How long do you keep paraffin blocks? 128 French labs



3 – Retrieval management



Saran: 100 000 m2 of storage for 8 million products: Only Amazon distribution center in France

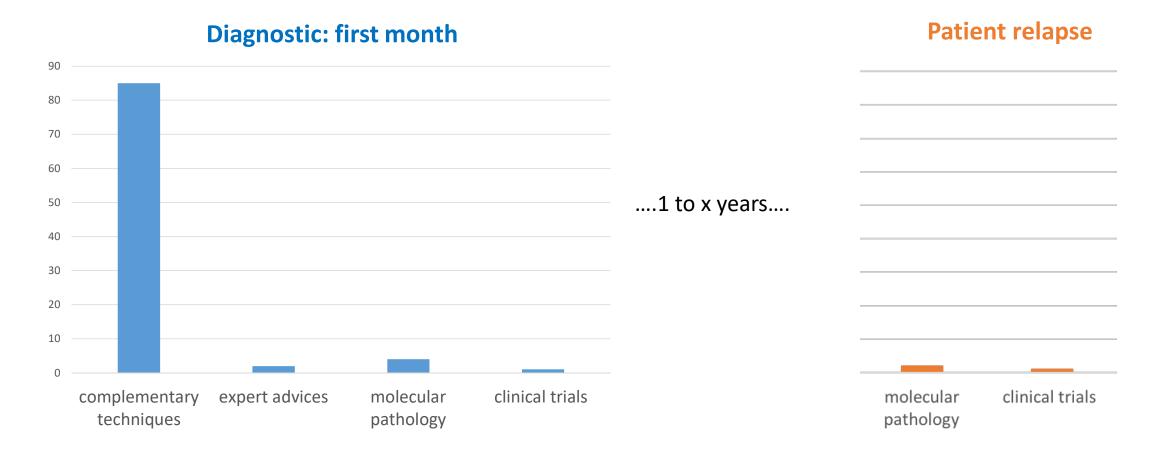
Why and when do we need to retrieve blocks?

• For diagnosis/Prognosis/therapeutic purposes:



Why and when do we need blocks?

• For diagnostic/Prognosis/therapeutic purposes:



• At any time: research, pedagogy... TRACEABILITY

- Mayo clinic: Tissue Registry Archives Warehouse
 - Since 1907
 - 15 Million slides, 6 Million paraffin blocks
- In 2005 they realized the following:
 - 300 000 blocks, 1 million slides were generated
 - 155,000 slides / 57,701 blocks were loaned out
 - 40% of slides and 54% of blocks not returned by the due date (2 mths)

- Issues identified:
 - large numbers of slides and blocks in separate tissue collections (5 investigators maintained 56% of the total number of blocks in their own lab)
 - inconsistent identification of the requesting physician/scientist
 - Transfer between investigators without sharing information back to Mayo
 - Investigators leave the institution with no follow-up back to Mayo...

- Implementation of a new tracking system with new policies:
 - who can borrow,
 - purpose of borrowed material (research, clinical, education, quality)
 - Time frames for return of material
 - Notification of overdue material
 - Penalties
- New procedures:
 - Mayo now makes investigators sign a verification form online;
 - the investigator must be authorized to request materials
 - have no overdue material outstanding Giannini C et al. Maintaining Clinical Tissue Archives and Supporting Human Research: Challenges and Solutions. Pathol Lab Med. 2011;135:347–353

• 2008: 206 330 slides and 51 416 blocks borrowed

- 94% of blocks and 93% of slides were returned
- lost: 44 slides and 25 blocks (< 0,05%)
- Staff members workload increased by 58% for slides and by 17% for blocks

Conclusion: improvement of traceability but with a large increase of resources

Giannini C et al. Maintaining Clinical Tissue Archives and Supporting Human Research: Challenges and Solutions. Pathol Lab Med. 2011;135:347–353

Release and return of archived diagnostic samples for clinical trials purposes

• Wherever possible, derived materials from a stored tissue block (e.g. tissue sections, extracted nucleic acids) should be provided, rather than the block itself

• At least one block of diagnostic tissue should be preserved for the minimal retention time of paraffin blocks and should not be used for research, education, quality control, or any other non-diagnostic activities.

Are There Barriers to the Release of Paraffin Blocks for Clinical Research Trials? A College of American Pathologists Survey of 609 Laboratories Arch Pathol Lab Med—Vol 135, July 2011

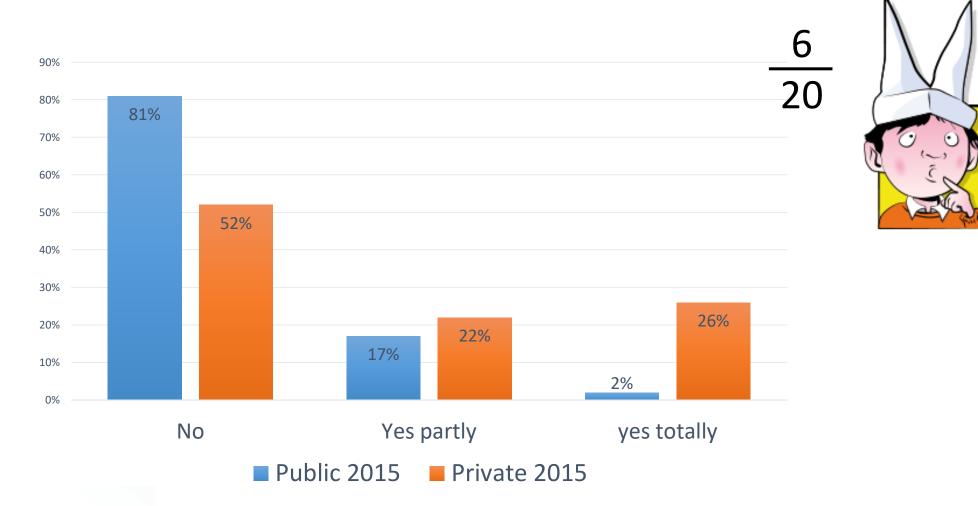
4 – long-term archiving: what cost?



Cellar of the "banque de France", property of the French republic: About 2500 tons of gold, 82 billion euros are kept less than 25 meters beneath the ground in the middle of a groundwater in Paris

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Do you know the cost of long term archiving in your lab?



ASSOCIATION FRANÇAISE D'ASSURANCE QUALITÉ EN ANATOMIE PATHOLOGIQUE

Our long term storage experience! About 2 Million blocks in a 60m2 (645sq feet) room: 20 years of archiving



LONG TERM ARCHIVING Cost of gathering 2M blocks (est 20 years)

Items	Core Archiving	TOTAL Cost (EURO)
Storage room 130 euros/m2/year 2 millions blocks in 60 m2	390 per year x20 years	81,510
Shelves, drawers and cardboards	13,000 x 20	260,000
Headcount 10 hrs/months	2,040 x20	40,800
TOTAL - EURO		382,310
TOTAL - USD		~ 400,000

DOES NOT INCLUDE ROUTINE MANAGEMENT – JUST LONG TERM ARCHIVING

LONG TERM ARCHIVING Ongoing costs 2M blocks – 100K per year

ltems	Core Archiving	Extra cost per year for new blocks	TOTAL per Year (EURO)
Storage room 130 euros/m2/year 2 millions blocks in 60 m2	7,800 (*increases every year)	390	8,190
Shelves, drawers and cardboards	0	13,000	13,000
Headcount 10 hours/months	0	2,040	2,040
TOTAL - EURO	7,800	15,430	23,230
TOTAL - USD	8,345	16,509	~ 25,000

Every 5 years about 125,000 USD of cost

DOES NOT INCLUDE ROUTINE MANAGEMENT – JUST LONG TERM ARCHIVING

Block archiving reimbursement?

- The AMA CPT system has a block retrieval code: 88363
 - "Molecular assays are now being used as a part of selecting specific antineoplastic treatment regimens, which require pathologists to retrieve previously diagnosed surgical pathology cases and determine appropriate material(s) for these assays."
 - Medicare Reimbursement for CPT 88363 includes a Medicare Non-Facility Payment of \$22.88 and a Facility Payment of \$19.67
- Long term archiving is an unfunded mandate for pathological labs

Tissue archiving: take home messages

• Identification:

- Use automatic labelers connected with LIS
- Avoid batch work
- Use two identifiers (accessioning number/bare code)

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- Minimal retention period: 10 years but tends to increase

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- Retrieval tracking:
 - Increase need to de-archive blocks
 - Difficult to improve without additional resources

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 - Increase need to de-archive blocks
 - Difficult to improve without additional resources
- Economical issue:
 - Very few data but more expensive than we think

Part 2: Evaluation of a new block management system

Our department of Biopathology

- 30 000 biopsies and surgical samples
- 10 000 cytological samples/year
- 110,000 paraffin blocks/year
- IHC, FISH, HRM, NGS..



- 17 + 4 technicians, 3 lab aids, 4 secretaries
- Biobanking: 4 people











Pilot site for testing automation of paraffin block management

- Medical Device Rating department
- Cooperation in the development (contract 8605 4/12)
- Testing of prototypes
- Installed in July 2014



Un réseau de moyens expérimentaux une expertise clinique, biologique et technique avec accès au patient



U | Oui sommes nous ?

La recherche au CHRU de Montpellier s'organise au sein de laboratoires, d'instituts, de centres de collections biologiques, implantés au cœur de l'établissement et dotés de moyens expérimentaux de pointe, servis par des équipes recomues.

Organisées en plateformes, ces ressources permettent aux équipes de progresser wers leurs objectifs de recherche, avec un accés au patient. Ces moyens sont ouvers aux partenariats publics et privés. Des équipements de demière génération accompagnés par une expertise médicale, biologique et technique sont proposés aux professionnels de la santé, aux équipes de recherche publiques et privées, aux partenaires industriels, aux aporteurs de projets, pour la mise en œuvre de collaborations de recherche et développement (méxol, la rehistant de prositions, la mise à disposition de ressources technologiques pour un essai clinique, ou le développement de banques de données cliniques.

Chaque plateforme produit une offre spécifique qui va de la réalisation d'une analyse ou d'un transfert de ressources biologiques pour la recherche, à la prise en charge de projets coliboratis. Elle intervent également dans des actions d'expertise-conseil, d'évaluation de dispositifs médicaux, de mise à disposition de moyens avec ou sans accompagnement, d'accueil d'entreprises èmergentes et de formations ciblées.

Ouelques mots clés

Analyse pangénome de l'expression des gènes, Analyses et expertise en protécmique chique, Cession de ressources biologiques humaines, Production de cellules souches pluripotentes induites, Analyse cytogénétique des cellules souches, Séquencage NGS, Protocoles de recherche clinique en imagine litM 31, Isolement et recuel de cellules spécifiques pour analyses ADN, Etudes en nutrition humaine, Agro-alimentaire, Collection de plus de 6500 souches de Leistmania, Exploration de la maladie résiduelle en cancérologie, Analyse lymphocytaire et quantification virale, limmuno-diagnostic, Vaccination anti tumorale, Isolement et cession d'ilots pancréatiques humains ...

Contact

Yves El KAIM, Coordonnateur des Plateformes de recherche Direction de la recherche et de l'innovation Tél: 04 07 33 09 50 Hópita la Colombiete Pavilon nº 32 - 39 avenue Charles Fishaut - 34295 Montpelier cedex 5 plateformes?bu-montpelier.fr

> Rendez-vous sur notre site http://www.chu-montpellier.fr/fr/plateformes



1 - Block management in our lab before automation



First step: block sorting

- blocks were sorted by numerical order in metallic drawers
- Drawers took up a lot of space
- Need to move a lot of blocks when large cases came in late (autopsies, fetal pathology, bone specimens)
- Risks for misfiling of the blocks



Second step: block retrieval

- Manual removal of blocks without securing adequate space for returning
- Manual retrieval and re-archiving
- Inconsistent use of block registry (only used for long term removal of blocks)

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IA. 1TU, 2A, 3TU, 4A	15	5 HE + 10 IHC	DR RANCHERE - LYON (CGEB)	AVIS	DR DELFOUR	22/12/2014
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1A			DR CAYE-EUDE (CGEB)	AVIS	DR ROUSSET	23/12/2014
1A TU			DR CAYE-EUDE (CGEB)	AVIS	DR ROUSSET	23/12/2014
10	2	2HE	PR CRIBIER - STRASBOURG (CGEB)	AVIS	DR DELFOUR	23/12/2014
	4	1 HE + 3 IHC	PR COINDRE - BORDEAUX	MDM2	DR RIGAU	05/01/2015
2F 2I 2J	21	9 IHC +12 HE	PR COINDRE - BORDEAUX	MDM2	DR DELFOUR	05/01/2015
1A	1	1HE	DR RANCHERE - LYON (CGEB)	Relecture	DR DELFOUR	06/0/12015
1A, TK, TK	14	3 HE + 11 IHC	DR RANCHERE - LYON (CGEB)	Relecture	DR DELFOUR	06/01/2015
1A, 1B	14	2 HE + 12 IHC	DR RANCHERE - LYON (CGEB)	Avis	DR DELFOUR	07/01/2015
1A	11	1 HE + 10 IHC	DR RANCHERE - LYON (CGEB)	Avis	DR DELFOUR	07/01/2015
1A	7	1HE+2colo+4IHC	DR MC GREGOR (CGEB)	AVIS	DR RAMOS	06/01/2015
1C	7	1HE+6IHC	Pr URO-COSTE (CGEB)	AVIS	DR RIGAU	06/01/2015
• H\ Explications \ AV	52	49IHC+3HE	PR LABROUSSE - LIMOGES	AVIS	DR RIGAU	07/01/2014





Old blocks to file but I don't know where they go?

Third step: final archiving

• Once a week, blocks were transferred from metal drawers into cardboard drawers for long term storage





Function	Tasks	FTE	
Lab Aids	 Block sorting Long term transfer Long term retrieval Manual register 		
Lab Technician	 Block research for complementary techniques Manual register 		
Secretaries	 Block research for external requests Database management 		
Pathologists	 Block research for educational and scientific works 		
TOTAL		1.4	

2 - Paraffin block automation





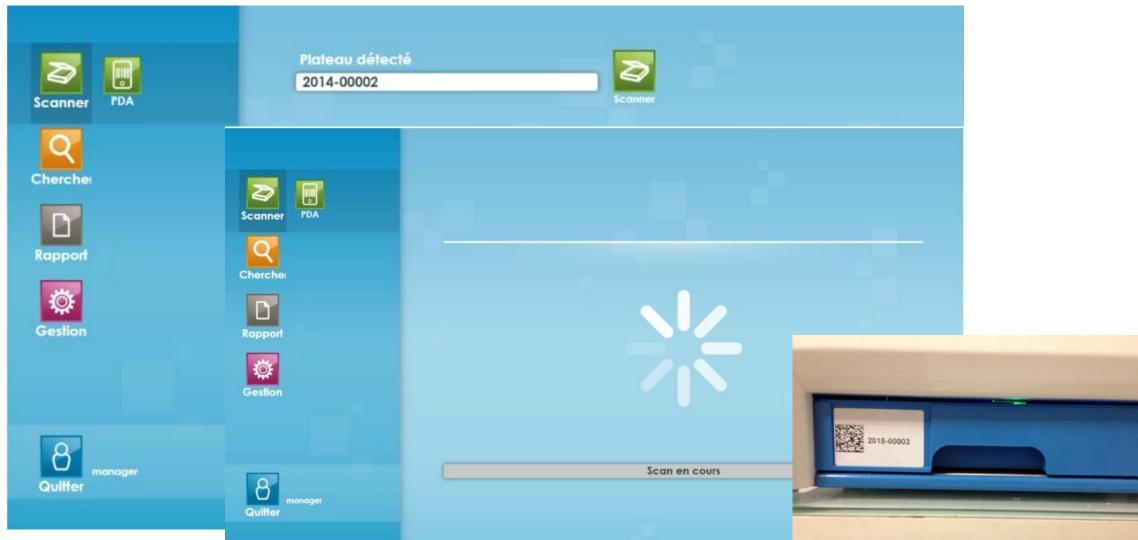


First step:

- the blocks are stored in a tray at the cutting station (240 blocks/tray).
- They are placed in the tray in any order (time-saving)
- Once the technicians have finished cutting they scan the tray in FINA



When we insert a new tray, the scanner will detect it and ask us to print a new label to stick on the tray

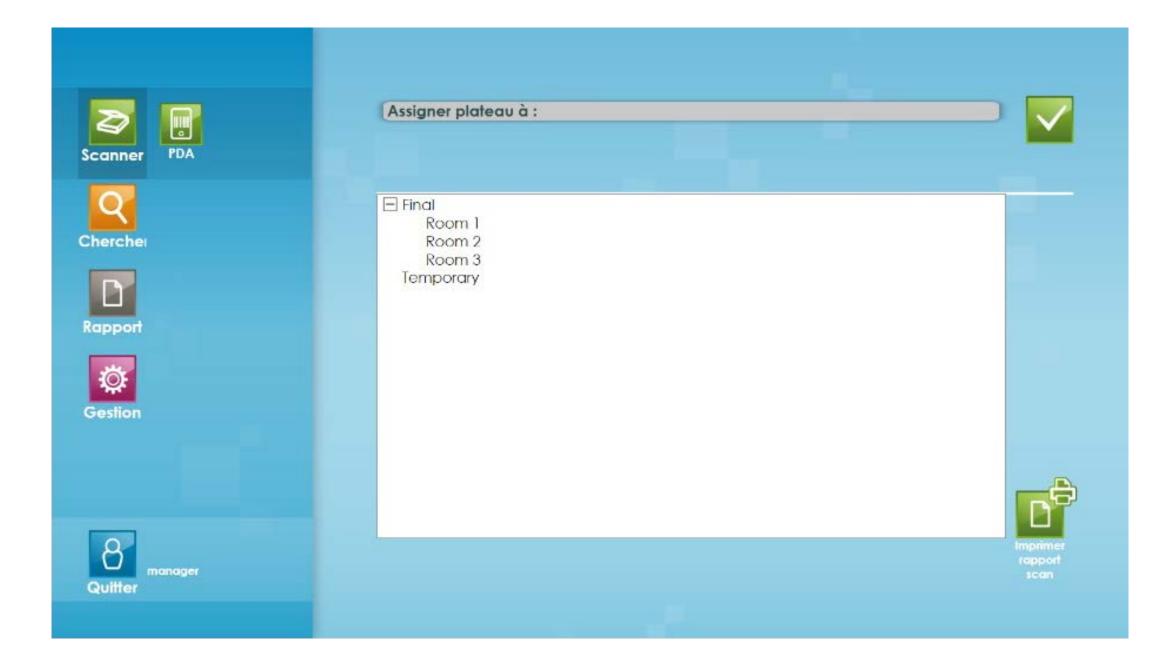


Scanning time varies from 2 to 6 minutes due to number of blocks, quality of printing and cleanness of the paraffin block.

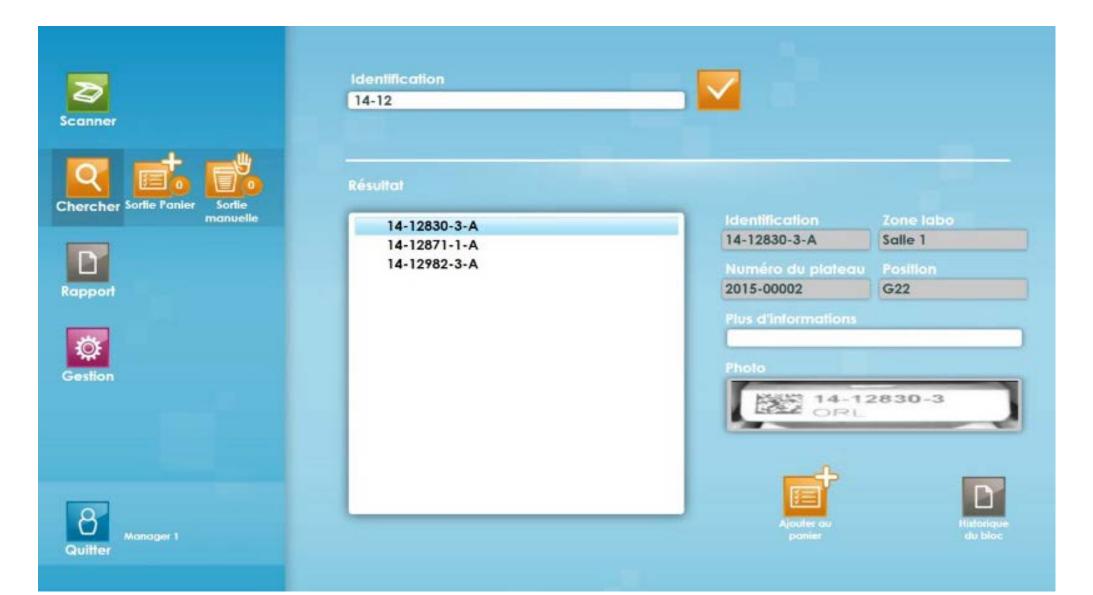
If the barcode is damaged, a picture of the block is taken and it can be entered manually in the software

Scan PDA	Enter block name
Search	Scan error Error counter
Report	Image: Sector of the sector
Manage	Image: Contract of the contra
Manager Log Off	Take new Photo
Log On	

Percentage of unread blocks: 242/26400 (< 1%) Primary reason: paraffin covering the barcode



2nd step: searching for blocks



Selected blocks are added to the picking list (1)

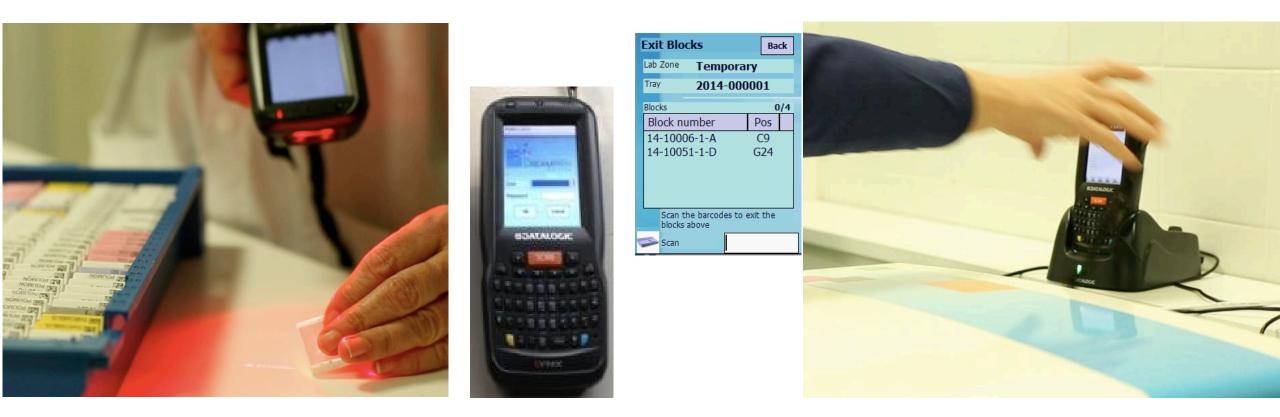
Scanner 2	Identification 14-12		
Cherche Sorie Panle Sorie Banuelle Rapport	Résultat 14-12830-3-A 14-12871-1-A 14-12982-3-A	Identification 14-12830-3-A Numéro du plateau 2015-00002 Plus d'informations Photo	Zone labo Salle 1 Position G22
Quitter Monager 1		1	Historique du bloc

Once the list is completed it's exported to the PDA (2)

For each block, we can log into the system the reason for removing it and the expected duration of time it will be out. Next, we can have alerts requesting any delays in re-archiving it



Blocks removed are scanned with the PDA ensuring all needed information is captured in the database



When ready to be returned, the pulled blocks are replaced in the current tray and re-scanned

3^{rd step}: long term storage

- We've created 2 storage zones
- Trays are stored in cabinets in the lab zone for 2 years
- Afterwards, we transfer the trays to cupboard sleeves in our long storage zone

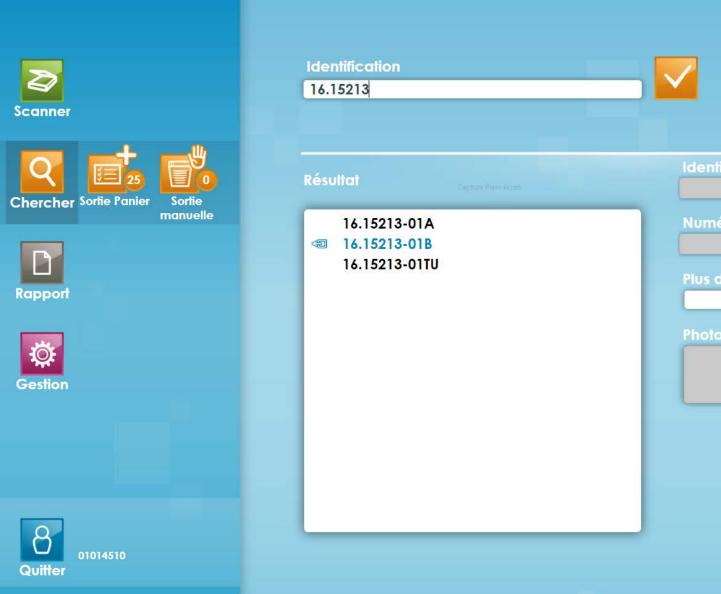


Saving of 1 FTE time

Function	Tasks	FTE	Impact Automation	New FTE
Lab Aids	 Block sorting Long term transfer Long term retrieval Manual register 		$\downarrow \downarrow \downarrow \downarrow$	
Lab Technician	 Block research for complementary techniques Manual register 		\downarrow \downarrow	
Secretaries	 Block research for external requests Database management 		Χ	
Pathologists	 Block research for educational and scientific works 		X	
TOTAL		1.4		0.4

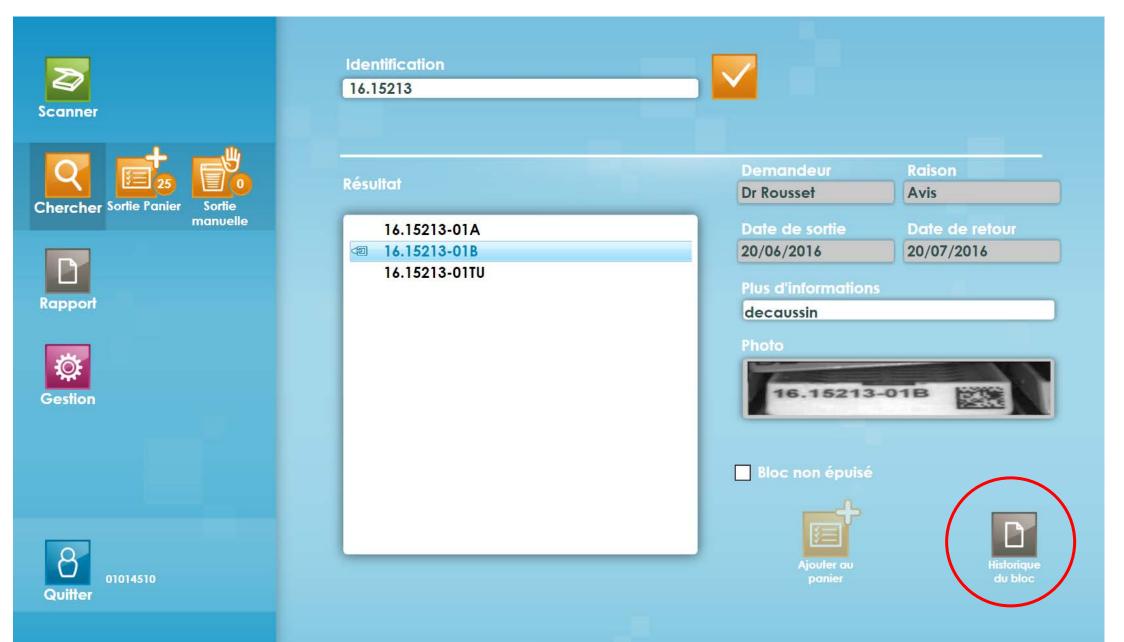
3 - Traceability

Block history



Identification Zone labo Numéro du plateau Position Plus d'informations Photo		
Plus d'informations Photo		Zone labo
Photo	Numéro du plateau	Position
	Plus d'informations	
	Photo	
Ajouter au <u>Historique</u>	Ajouter au	Historique

Block history



Block history



Scanner







Quitter

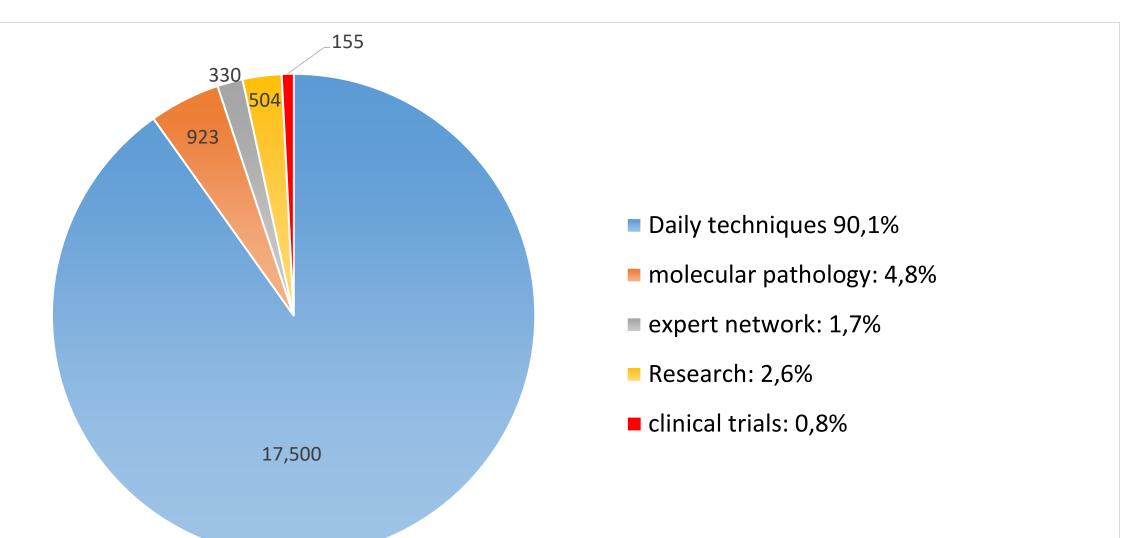
Rapport

Historique du bloc





How many blocks did we retrieve in 2016? And why?



About 20% (19412) of blocks were retrieved in 2016 so a tight management is needed

Due blocks out of the system at the end of 2016

- Second Opinion, expert consultation: 138
- clinical trials: 45
- External research (biobank): 29 (+ 360 definitive exits)
- Internal research: 75
- Externalized techniques: 16
- Blocks used for positive controls: 4

With information about the recipient, the protocol number etc....

In conclusion



• Gain of resources

- we are saving 1 FTE in time savings
- we are working on the connection of FINA to Our LIS

Block traceability

- Know where blocks are at all times
- Who, when and why
- Reduces errors

• Frees up space in the lab

• 4 linear meters

Improves safety and regulatory

- Minimizes risk of loss
- Allows for block QC
- Unique tray for long-term storage