# e-POSTERS

## e-Posters Morning Session:


The prognostic value of the VEGFR-1 and -2 combinations in endothelial cells of colorectal cancer.


Expression of the small GTPase Rab27B is associated with stromal inflammation in ductal carcinoma in situ of the breast.

**P 03** Herbelet S., Beck I., Dredert Z., De Wever O., De Bleecker J. / UZ Gent

NFAT5 forms aggregates in normal and Duchenne muscular dystrophy cultured myotubes after exposure to cell stressors.


Genomic profiling of lung cancer cytological samples using next generation sequencing.


Densitometry of Feulgen-stained histological sections helps to diagnose partial hydatidiform mole.

**P 06** Trépant A., Le Mercier M., Maris C., De Nève N., Blanchard O., D’Haene N., Salmon I. / ULB Erasme

Clinical application of targeted next generation sequencing for glioblastoma patients.

**P 07** D’Hondt D., Dendooven A., Jacobs W. / UZ Antwerpen

CASE REPORT: Postmortem diagnosis of phenytoin associated reactive lymphadenopathy.

**P 08** Henry P., Vanderveken J., Stevens M., Dubois D., Guiot Y., Jouret-Mourin A. / UCL Saint-Luc, Brussels

Concomitant HER2 immunohistochemistry (IHC) and in situ hybridization (ISH) detection in gastroesophageal junction and gastric adenocarcinoma : beneficial or not?

**P 09** Eerdekens A., Simoens C., Schoolmeesters O., Bogers J.P. / University of Antwerp

Molecular markers for invasive uterine cervical cancer: systematic review.

**P 10** Yves Sucaet, Silke Smeets, Stijn Piessens, Sabrina D’Haese, Chris Groven, Wim Waelput, Peter In’t Veld / UZ Brussel

Building a digital pathology ecosystem for education and research.
### e-Posters Afternoon Session:

| P 12 | Verbeke H., Ghislain V., Coucke W., Van Campenhout C., Van de Walle P. / Scientific Institute of Public Health, Brussels | Evolution of the implementation of a quality management. | 165 |
| P 13 | Hastir D., Buggenhout A., Simon P., Remmelink M., Noël J. / ULB Erasme, Brussels | CASE REPORT: Malignant transformation of a prior multicystic peritoneal mesothelioma with a follow-up of 7 years. | 167 |
| P 14 | Steelandt T., Ceulemans L., De Hertogh G., Pirenne J. / UZ Leuven | CASE REPORT: Intestinal graft loss following usage of nonsteroidal anti-inflammatory drugs. | 168 |
| P 15 | Steelandt T., Ceulemans L., De Hertogh G., Claes K., Monbaliu D., Pirenne J. / UZ Leuven | CASE REPORT: Combined kidney and intestinal transplantation as a treatment for secondary hyperoxaluria. | 169 |
| P 16 | Van Renterghem S., Himpe E., Ruige J., Huvenne W., Van Dorpe J., Praet M. / UZ Ghent | CASE REPORT: Thyroid nodules: rare events of metastatic invasion of RCC. | 170 |
| P 17 | Fontanges Q., Heimann P., Salmon I. / ULB Erasme, Brussels | CASE REPORT: A challenging diagnosis for the pathologist: NUT midline carcinoma. | 171 |
| P 19 | I. Benoy, D. Vanden Broeck, J. Bogers/ AML, Sonic Healthcare, Antwerp | Technical evaluation of Qvintip self-collected samples on Abbott high-risk HPV and AML qPCR HPV test. | 175 |
P 01
THE PROGNOSTIC VALUE OF THE VEGFR-1 AND -2 COMBINATION IN ENDOTHELIAL CELLS OF COLORECTAL CANCER


Introduction:

Research on tumour angiogenesis has mainly focused on vascular endothelial growth factor (VEGF) family and methods to block its actions. However, reports on the VEGF receptor (VEGFR) expression in tumor-associated endothelial cells (EC) are limited.

Aim:

We decided to evaluate immunohistochemical VEGFR1 and VEGFR2 expression in EC of colorectal cancer (CRC).

Methods:

EC VEGFR1 expression was quantitatively evaluated by computer-assisted microscopy in a retrospective series of 259 tumor tissues. Results were related to clinical variables.

Results:

The data show that the EC VEGFR1 and VEGFR2 expression are heterogenous. Using univariate analysis, high EC VEGFR1 expression is an independent negative prognostic factor in terms of metachronous metastasis (p = 0.031) and overall survival (p = 0.004). Low EC expression of VEGFR2 is an independent negative prognostic factor in terms of metachronous metastasis (p = 0.043). The combination of high VEGFR1 and low VEGFR2 is associated with improved metastasis-free survival (p = 0.005) and improved overall survival (p = 0.04). Using multivariate analysis, high EC VEGFR1 expression is still an independent negative prognostic factor associated with poor overall survival. The combination of high VEGFR1 and low VEGFR2 is an independent negative prognostic factor with regard to metastasis-free survival (p = 0.007) and overall survival (p = 0.012).

Conclusions:

This work illustrates the importance of studying distribution of VEGF members in EC of CRC. Interestingly, higher EC VEGFR1 expression and lower EC VEGFR2 expression appears as being involved in CRC progression, suggesting that targeting EC VEGFR1 could offer novel opportunities for CRC treatment.
P02

Expression of the Small GTPase Rab27B is Associated with Stromal Inflammation in Ductal Carcinoma in Situ of the Breast


Introduction:

Ductal carcinoma in situ (DCIS) is regarded to be a non-obligate pre-invasive precursor of invasive ductal carcinoma. Some DCIS present with an inflammatory infiltrate in the periductal stroma, but the etiology of this stromal inflammatory response is currently unknown. Rab27B is a small GTPase that is involved in the release of exosomes, i.e. small intraluminal vesicles that are released upon fusion of multivesicular endosomes with the plasma membrane. Rab27B is upregulated in invasive ductal carcinoma, but its role in early breast cancer progression and the tumor immune microenvironment is still relatively unexplored.

Aim:

We aimed to investigate Rab27B expression in DCIS, as well as its relation with stromal inflammation.

Methods:

Investigations were performed on a cohort of 71 consecutive patients diagnosed with pure DCIS. The following histopathological features were assessed: DCIS architecture, nuclear grade, calcifications, extensive comedonecrosis, apocrine differentiation and peritumoral stromal inflammation. Immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR) and Rab27B was performed on whole mount slides. HER2 amplification status was determined by dual-probe fluorescence in situ hybridization (FISH). Chi-square test and multivariate logistic regression analysis were performed to analyze which features were associated with stromal inflammation.

Results:

Thirty-five of 79 DCIS (49%) presented no or mild stromal inflammation, and 36 of 79 DCIS (51%) showed moderate to extensive inflammation in the periductal stroma. High nuclear grade (p<0.001), absence of intraductal calcifications (p=0.042), presence of extensive comedonecrosis (p<0.001), Rab27B overexpression (p=0.048), ER negativity (p=0.007) and PR negativity (p<0.001) were significantly associated with the presence of moderate to extensive stromal inflammation. DCIS architecture (p=0.559) and apocrine differentiation (p=0.305) were not associated with stromal inflammation. In multivariate analysis, high nuclear grade (p=0.005), HER2 amplification (p=0.002) and high Rab27B expression (p=0.007) were independently associated with the presence of moderate to extensive stromal inflammation in DCIS.
Conclusions:

We aimed to explore the underlying causes of stromal inflammation in DCIS. We have shown that DCIS lesions with moderate to extensive stromal inflammation present more often high nuclear grade, HER2 amplification and Rab27B overexpression. Rab27B is a secretory GTPase involved in vesicle trafficking and exocytosis. Secretory products of malignant epithelial cells might evoke a host inflammatory response in the tumor microenvironment. Further research is necessary to elucidate which secretory products might be responsible for this inflammatory response. Additional studies are required to investigate whether the presence of stromal inflammation and Rab27B overexpression are markers of poor prognosis in DCIS.
NFAT5 FORMS AGGREGATES IN NORMAL AND DUCHENNE MUSCULAR DYSTROPHY CULTURED MYOTUBES AFTER EXPOSURE TO CELL STRESSORS.


Introduction:

Like myodegeneration and fibrosis, Duchenne muscular dystrophy (DMD) is also characterized by chronic inflammation. In DMD, dystrophin malfunction causes Ca2⁺ and Na⁺ influx, which is deleterious to DNA. Nuclear factor of activated T-cells 5 (NFAT5) is upregulated and translocated to the nucleus in cells exposed to extracellular hyperosmolarity and the accompanying Na⁺ influx. In turn, NFAT5 induces the production of osmolytes which will restore cell homeostasis. NFAT5 is also activated by cytokines IL-1β and TNF-α.

Aim:

This study aims to understand the impact of cytokines IFN-γ, IL-1β and TNF-α and of increasing NaCl concentrations on NFAT5 expression and localization in normal and in Duchenne muscular dystrophy cultured myotubes.

Methods:

Myoblasts were grown in DMEM containing high glucose, additionally supplemented with 10% fetal calf serum, penicillin + streptomycine. After differentiation to myotubes, cells were exposed to cytokines IFN-γ, IL-1β and TNF-α or mixtures thereof. Increasing NaCl concentrations from 18mM to 100mM were added to the cultures. NFAT5 localisation and expression were studied by means of immunofluorescence (IF), Western-blotting and qPCR.

Results:

Our findings demonstrate that NFAT5 is mildly, yet consistently upregulated and is induced to form aggregates in normal and DMD myotubes after exposure to increasing hyperosmolar NaCl concentrations or cytokines IL-1β, IFN-γ and TNF-α or mixtures of these cytokines. These cytoplasmic aggregates accumulate in the perinuclear region of the cell. IF seems to colocalize NFAT5 aggregates with ubiquitin, whereas IF for markers of the Golgi apparatus and endoplasmic reticulum did not show any co-localization with the NFAT5 aggregates. IF staining of biopsies of patients suffering from DMD, dermatomyositis or polymyositis revealed NFAT5 aggregates accumulating around the myonuclei, resembling the picture obtained with our salt- or cytokine-induced myotubes. In chronic myositis as well as in muscular dystrophy with bystander inflammation, such as in DMD, abnormal NFAT5 proteomics may be a crucial component of interactions between inflammatory and degenerative pathomechanisms.

Conclusions:

The data help to better understand the pathology of muscular dystrophy as well as myositis.
Introduction:

NCCN guidelines recommend broader molecular profiling to identify rare actionable mutations for lung cancer patients. Next generation sequencing (NGS) has begun to supplant other technologies for gene panel sequencing. Cytological sample is sometimes the only material available for diagnosis of lung cancer. Therefore, molecular testing should be also validated on cytological samples, such as fine needle aspiration or pleural effusion.

Aim:

In the present study we evaluate the clinical applicability of targeted NGS on cytological lung cancer samples.

Methods:

The DNA of 93 formalin-fixed paraffin-embedded cell blocks was prospectively subjected to targeted NGS with the Ion Torrent AmpliSeq colon/lung cancer panel which interrogates 1850 hotspots in 22 cancer-related genes using the Ion Torrent Personal Genome Machine.

Results:

The set of 93 samples included 8 primary tumors and 85 metastatic lesions. Eighty-seven (94%) samples were adenocarcinomas. Eighty-five (91%) samples were successfully sequenced. The most frequent mutations were found in TP53 (49%) and KRAS (37.6%). Twenty potentially actionable mutations were identified (23.5 %), including 11 EGFR mutations, 2 PIK3CA mutations, 5 BRAF mutations, 1 PTEN mutation and 1 NRAS mutations.

Conclusions:

Overall, the AmpliSeq colon/lung cancer panel can be applied in daily practice for cell blocks. Moreover, it provides clinically relevant information for lung cancer patients.
P 05
DENSITOMETRY OF FEULGEN-STAINED HISTOLOGICAL SECTIONS HELPS TO DIAGNOSE PARTIAL HYDATIDIFORM MOLE.

Introduction:
Partial hydatidiform mole (PHM) is associated with triploidy or tetraploidy that can be diagnosed by caryotype analysis. However, material is not available for genetic analysis in many instances of miscarriage and only formalin-fixed and paraffin-embedded (FFPE) material can be used to reach a diagnosis. Histopathological diagnosis of PHM is not easy because morphological features may overlap with hydropic miscarriages associated or not with other genetic anomalies and immunohistochemistry is of no help, leading to high interobserver and intraobserver variability. Patients with PHM are at risk for subsequent molar pregnancy or trophoblastic gestational disease, even if the risk is lower than for complete hydatidiform mole (CHM). We therefore think there is a need for a convenient tool to improve the diagnosis in routine pathological work.

Aim:
We wanted to develop a morphometric method that could help to diagnose PHM on FFPE miscarriage products with no available caryotype.

Methods:
74 FFPE samples of PHM, CHM, diploid miscarriages and miscarriages suspected to be PHM but without caryotype were used in the study. Sex chromosomes were labelled by fluorescent in situ hybridization in miscarriages with unknown caryotype. Histological sections were stained according to Feulgen or with 4',6-diamidino-2-phenylindole (DAPI). Optical density and area of nuclear profiles were measured on Feulgen-stained histological sections. Fluorescence level was measured on DAPI-stained histological sections.

Results:
Optical density, nuclear area, and their product were largely increased in stromal cells of chorionic villi in PHM compared to diploid cases and maternal endothelial cells. Optical density was also lower in decidual cells but nuclear profile area was larger, preventing to use these cells as diploid control. Feulgen densitometry also strongly supported triploidy in miscarriage products with 3 sex chromosomes compared to those with 2 sex chromosomes. DAPI fluorescence levels yielded similar results.

Conclusions:
Feulgen densitometry is an easy-to-use method that allows to confidently diagnose PHM on FFPE miscarriage products with no available caryotype.
Introductory:

Glioblastomas (GBMs) are the most common malignant primary brain tumours in adults. These tumours are resistant to conventional treatment approaches including surgical resection, radiotherapy and chemotherapy. International efforts to catalogue mutations for multiple forms of cancer coupled with the successes of targeted agents in patients with molecularly defined tumors and improvements in genomic technology have generated enthusiasm for incorporating genomic profiling into clinical cancer practice. The development of tyrosine kinase inhibitor treatments has made it important to test cancer patients for clinically significant gene mutations that influence the benefit of treatment. Therefore, the number of biomarkers that will need to be assessed is expected to increase rapidly. Recently, next generation sequencing (NGS) has begun to supplant other technologies for gene panel sequencing. However, few studies have validated the use of targeted NGS for GBM patients. In the present study we evaluate the clinical applicability of targeted NGS for patients with GBM.

Methods:

DNA from 59 GBM samples was retrospectively subjected to targeted NGS with the Ampliseq Cancer Hotspot Panel, using the Ion Torrent Personal Genome Machine, which allowed us to analyze 2850 known cancer-related mutations in 50 genes and copy number variation for 24 genes. In addition, MGMT methylation status was evaluated by Methylation Specific PCR. All samples were successfully sequenced.

Results:

The most frequent mutations were found in TP53 (25%), and EGFR (17%). Potentially actionable mutations including 10 EGFR, 2 PIK3CA, 5 PTEN, 1 BRAF, 1 KRAS, 1 PDGFRA and 4 IDH1 mutations were identified in 22 patients (37%). Moreover, PDGFRA, MET and EGFR amplifications were detected for 11 (19%), 13 (22%) and 27 (46%) patients respectively.

Conclusions:

Overall, the AmpliSeq Cancer Hotspot Panel can be applied in daily practice for GBM samples. Moreover, it can provide clinically relevant information for GBM patients.
P 07
CASE REPORT
POSTMORTEM DIAGNOSIS OF PHENYTOIN ASSOCIATED REACTIVE LYMPHADENOPATHY.

Content:
Phenytoin is sometimes still used as an anticonvulsant in the treatment of epilepsy. It is known to cause side effects and hypersensitive reactions. We present a case report of a 27-year-old man who died under suspicious circumstances in his hotel room after feeling sick during the day. He was known to be treated for epilepsy with Phenhydan®100 mg. A forensic autopsy was performed to exclude an unnatural cause of death.

The following autopsy findings were noted: gingival hyperplasia, ulceration of the laryngeal mucosa, acute lung congestion and enlarged thoracic and abdominal lymph nodes. Tentative autopsy diagnosis was “lymphoma”. A detailed histological examination and immunophenotyping were performed on the enlarged lymph nodes. A paracortical expansion by a polymorphous population of immunoblasts (B-cells), plasma cells, histiocytes and cells mimicking Reed-Sternberg cells were seen. Immunophenotyping showed an intact immunoarchitecture and was used to exclude malignant lymphoma. In this case the diagnosis of a phenytoin-associated reactive lymphadenopathy was made. A further discussion of the clinical and histological findings will be presented.
CONCOMITANT HER2 IMMUNOHISTOCHEMISTRY (IHC) AND IN SITU HYBRIDIZATION (ISH) DETECTION IN GASTROESOPHAGEAL JUNCTION AND GASTRIC ADENOCARCINOMA: BENEFICIAL OR NOT?


Introduction:

Background

HER2 analysis in gastroesophageal junction (GEJC) and gastric adenocarcinoma (GC) is required to predict patients' responsiveness to trastuzumab therapy. The current Belgian recommendations for HER2 testing include IHC followed by systematic ISH. Here, we compare the results between IHC and SISH in 221 cases of GEJC and GC.

Methods:

Materials and method

221 cases of GEJC (n=71; 6 poorly cohesive carcinoma (PCC) and 65 intestinal type (IT)) and GC (n=150; 42 PCC and 108 IT), collected over a period of 2 years (01/2013-03/2015), were tested by both IHC (clone 4B5, Ventana) and SISH (brightfield in situ hybridization; Inform Her2) using benchmark Ventana.

Results:

When using concomitant IHC and SISH, HER2 positive rates in GEJC and GC were 29,2% and 17,6% respectively. The concordance of results for HER2 amplification status between IHC and SISH was 95,4% (211/221). Amongst the 10 discordant cases, 9 were false positive results (IHC: 3+ SISH: -), corresponding to 6/25 cases of GC and 3/22 cases of GEJC. Only one false negative result (IHC: 0 SISH: +) was observed in a GEJC case.

Equivocal cases following the European Guidelines (IHC: 2+) were SISH+ in 7/25 of GEJC and 6/47 of GC.

Conclusions:

Some discrepancies were observed when comparing IHC and SISH for HER2 testing.

False positive results by IHC may be caused by misinterpretation of staining or sampling errors, etc. Systematic execution of ISH, as mentioned in the Belgian guidelines, tends to improve the quality of the results.
P 09
MOLECULAR MARKERS FOR INVASIVE UTERINE CERVICAL CANCER: SYSTEMATIC REVIEW

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Introduction:
A large number of studies have investigated the occurrence of different tumor-associated antigens on invasive squamous uterine cervical cancer.

Aim:
This systematic review is a preliminary study to distinguish peroperatively invasive uterine cervix tumors from normal cervical squamous epithelium with the aid of tumor-associated antigens. The aim is to produce an evidence based list of tumor-associated antigens specific for invasive squamous uterine cervix tumors and displaying their diagnostic accuracy (sensitivity and specificity).

Methods:
A literature search was performed in Medline (via PubMed), Cochrane Register of Diagnostic Test Accuracy Studies and Web of Knowledge. Only studies that met the predetermined inclusion criteria were included in the analysis. Study quality was assessed using QUADAS (Quality Assessment of Diagnostic Accuracy Studies).

Results:
The literature search resulted in 1012 articles. After selection based on title and abstract 637 articles could be excluded, 323 articles could be excluded after analyzing inclusion criteria. Four articles were included based on expert knowledge and 13 articles remained inaccessible. Data extraction and assessment of study quality was performed for the retained 43 articles. The tumor-associated antigens, described in these 43 articles, were classified according to the six biological properties that tumor cells can obtain during carcinogenesis. For each of these markers the sensitivity and specificity were displayed.

Conclusions:
In this systematic review p16INK4a, survivin, PCNA, Laminin 5 and VEGF were designated as tumor-associated antigens with the best diagnostic accuracy to diagnose invasive squamous uterine cervical tumors and distinguish them from normal cervical epithelium.
P 10
BUILDING A DIGITAL PATHOLOGY ECOSYSTEM FOR EDUCATION AND RESEARCH.
Yves Sucaet, Silke Smeets, Stijn Piessens, Sabrina D’Haese, Chris Groven, Wim Waelput, Peter In’t Veld / Department of Pathology, Faculty of Medicine, Vrije Universiteit Brussel

Abstract:
Successful roll-out of digital histopathology requires more than a whole slide scanner. At Brussels Free University (VUB), we currently have two main use cases for whole slide imaging: education and biobanking. Both are presented to various end-users through customized user interfaces. With the help of the Pathomation software platform for digital microscopy, these integrate various datastores and image repositories, where possible. Custom coding is used to interact with various vendor-software and server applications, where needed, and always with the goal of minimal data duplication in mind. The end-result is an interconnected network of heterogeneous information silos, and a thriving environment for multi-disciplinary and integrated (both brightfield and fluorescent) virtual microscopy. A subset of applications are available to the public via http://www.diabetesbiobank.org.
P 11
AUTOMATED ANALYSIS OF PROLIFERATION AND APOPTOTIC MARKERS IN PAPILLARY THYROID CARCINOMA


Introduction:

Proliferation and apoptosis are opposing processes by which the cell numbers are kept in a delicate balance, essential for tissue homeostasis, whereas uncontrolled growth of cells is a hallmark of cancer. Papillary thyroid cancer (PTC) is the most common type of thyroid cancer, accounting for 85-90% of all thyroid malignancies. Some PTC seem to follow an indolent course whereas other ones are metastatic and hence, more rapidly progressing tumours. We wanted to investigate whether proliferation and apoptotic markers could help to predict the biological behaviour of different types of PTC.

Aim:

Our aim was to evaluate respective contribution of proliferation and apoptosis in the tumorigenesis of papillary thyroid carcinoma (PTC) by automated analysis. This is the first study of its type which provides an automated assessment of the proliferative capacity and apoptotic potential of cells in PTC, covering the entire spectrum of lesions from ‘well differentiated tumour of uncertain malignant potential’ (WDT-UMP) to papillary microcarcinoma (PMC), follicular variant of PTC (FVPTC) and finally, metastatic PTC.

Materials and methods:

We investigated the immunolabelling of Ki67, phosphorylated histone H3 (pHH3), cyclin D1, active caspase-3, bcl-2, and p53 in thirteen cases each of metastatic PTC, FVPTC, PMC and WDT-UMP. Slides were scanned followed by digitalization of slides at a 20x magnification by SCN400 slide scanner (Leica, Wetzlar, Germany). The tumour tissue on each slide was delineated manually and scanned slides were then scrutinized using Tissue IA (Leica Biosystems, Dublin, Ireland). Colour deconvolution was applied using haematoxylin and DAB matrices of the software. Nuclear algorithms were applied for Ki67, cyclin D1, p53 and pH3 immunostaining, keeping the parameters constant for all slides. Cytoplasmic algorithms were applied for bcl 2 and caspase-3 immunolabelling, and the analysis was performed at 20 x magnification.
Results:
Out of the 13 FVPTC cases, seven were encapsulated and six were unencapsulated FVPTC. Ki67 was immunolabelled in more cells of metastatic PTC than of all other types and pHH3 was immunolabelled in more cells of metastatic PTC than of PMC. There was no significant difference between the proportion of cells immunolabelled for Ki67 and pHH3 in the unencapsulated FVPTC and the metastatic PTC. No difference was found for cyclin D1 immunolabelling between the PTC variants. Surprisingly, metastatic PTC and unencapsulated FVPTC also demonstrated more p53 and cleaved caspase-3 immunolabelled cells than other types. In contrast, increased expression of bcl-2 protein was seen in normal thyroid areas, encapsulated FVPTC and PMC as compared to WDT-UMP and metastatic PTC. Metastatic PTC shows higher proliferation than other types of PTC but unexpectedly also higher apoptotic levels. Similar results were also seen with unencapsulated FVPTC, thus demonstrating the fact that unencapsulated FVPTC indeed has a potential for adverse outcome.

Conclusions:
The progress of malignancy can be well tracked by assessing the proliferative/apoptotic number of cells in PTC. The expression of proliferative proteins, Ki67, pHH3 and cyclin D1 in particular, in PTC may indicate an aggressive behaviour by the tumour and loss of apoptosis inhibition by bcl-2 protein can further amplify the role of these proteins in tumour progression. Bcl-2 could prove an interesting marker of PTC precursor lesions. Automated/digital image quantification approach helps in refining the diagnostic accuracy.
P 12
EVOLUTION OF THE IMPLEMENTATION OF A QUALITY MANAGEMENT SYSTEM IN THE BELGIAN LABORATORIES FOR ANATOMIC PATHOLOGY
Quality of Medical Laboratories, Scientific Institute of Public Health, Brussels

Introduction:
The Royal Decree (RD) of the 5th December 2011, concerning the licenses of anatomic pathology laboratories came into force the 1th March 2013. The purpose of this RD is to monitor and guarantee the quality of the Belgian laboratories for anatomic pathology. Since the 1th March 2014 all Belgian anatomic pathology laboratories are licensed. Within the framework of this licensing the laboratories are obliged to elaborate a quality management system within five years. However, the requirements concerning topics like access/safety and hygiene, maintenance and calibration of equipment, management of quality documents and method validation, transmission and confidentiality of patient reports, content of patient reports and management and validation of computerized systems as stated in the articles 22, 24, 26, 27, 28 and 29 of the RD, respectively, should be fulfilled within a time period of three months counting from the entry into force of the license. Additionally, participation in the national external quality assessment program organized by the Belgian Scientific Institute of Public Health (IPH) is also required by law.

Aim:
In order to follow up the implementation of the quality management system and the implementation of the articles 22, 24, 26, 27, 28 and 29 of the RD in the Belgian anatomic pathology laboratories, a documentary audit by the department Quality of Medical Laboratories at the IPH has been performed.

Methods:
In 2014, in collaboration with the commission of anatomic pathology, all licensed laboratories were asked to fill out a table in which the percentages of implementation of each article (22/24/26/27/28/29) had to be indicated. In addition, the laboratories were requested to indicate for each item and article the corresponding Standard Operating Procedures (SOPs) and validity date.
In the course of 2015, during a second evaluation step, the laboratories were asked to actualize the table presented in the survey of 2014. In addition, some specific quality documents were requested as well, in particular the patient reports and the SOPs concerning the management of the quality documents and on equipment management.
The tables, patient reports and SOPs were evaluated substantively for the presence of predefined items after which the percentage implementation for each article (only for the evaluation of the tables) and an overall score were calculated.
**Results:**

From the installation of the RD till 2015, the number of licensed laboratories diminished from 102 in 2013 to 85 in 2015, mostly due to cessation of laboratories of connexist (specialist physicians who perform acts of anatomic pathology exclusively for their own patients).

In 2014, 96 laboratories were included in the evaluation survey and 59 participants (61%) obtained an overall implementation score (all articles includes) of more than 70%. During the second evaluation survey organized in 2015, among the 85 included laboratories, 77 (80%) received an overall implementation score of more than 70%.

In 2014 we counted 16 laboratories (16.6%) with an overall score of less than 25% as compared with 2015, in which no single laboratory scored less than 25%.

More detailed analysis of the obtained information revealed that the procedures on validation of methods and on management and validation of computerized systems seemed to be an issue. In 2014, only 56% of all laboratories had completely implemented the SOP on validation of methods, in contrast with 73% of the laboratories in 2015. In particular the implementation of article 29 (management and validation of computerized systems) seems to remain the biggest obstacle as only 30% of the laboratories had completely implemented this article in 2014 and still one third of all the laboratories are lacking this procedures in 2015.

**Conclusions:**

The collaboration with the laboratories has contributed to the awareness of the laboratories to work in a quality environment. Close monitoring, adjustment and support by the IPH and the commission of anatomic pathology improved and is still improving the implementation of a quality management system as stated in the RD on licensing conditions of the Belgian laboratories for anatomic pathology.
P 13

CASE REPORT

MALIGNANT TRANSFORMATION OF A PRIOR MULTICYSTIC PERITONEAL MESOTHELIOMA WITH A FOLLOW-UP OF 7 YEARS

Hastir D. (1), Buggenhout A. (1), Simon P. (1), Remmelink M. (1), Noël J. (1) / [1] ULB/Erasme Hospital, Brussels,

Content:

Multicystic peritoneal mesothelioma (MCPM) is a rare lesion occurring most frequently in young women and located in the pelvic mesothelium. This lesion is considered by some authors as a non neoplastic reactionnal mesothelial proliferation but others support that it is a borderline lesion with a tendency to recur after resection, that could be in rare case responsible of lymph node involvement and more rarely that could underwent malignant transformation. In the present study, we report a case of a 43-year-old female with a previous resected MCPM lesion located in the visceral pelvic peritoneum with an actual local recurrence and a transformation into low grade malignant mesothelioma. Our data are discussed according to a literature review of such rare cases previously described.
P 14

CASE REPORT

INTESTINAL GRAFT LOSS FOLLOWING USAGE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS.


Content:

In the last 2 decades, intestinal transplantation has emerged as a valuable life-saving treatment option for patients with intestinal failure and severe complications of total parenteral nutrition. Improved graft survival and quality of life allow recipients to return to their normal daily activities. Due to the unique immunological properties of the intestine, recipients have only a narrow window between infection and rejection. Exogenous factors disturbing the delicate immunologic balance can have a devastating effect. We present a case where the intake of a nonsteroidal anti-inflammatory drug for an orthopedic complaint eventually led to loss of the intestinal graft.

Notification:

This case has already been published in Transplantation in March 2015.
P 15
CASE REPORT
COMBINED KIDNEY AND INTESTINAL TRANSPLANTATION AS A TREATMENT FOR SECONDARY HYPEROXALURIA.

Content:
Intestinal transplantation is currently restricted to patients with irreversible small bowel failure who suffer from severe complications of total parenteral nutrition. On the other hand, kidney transplantation is the treatment of choice for end-stage renal disease. Certain intestinal diseases, like extensive intestinal resections, chronic inflammatory bowel disease and other malabsorption syndromes can cause enteric hyperoxaluria which in time will lead to end-stage renal disease. In order to prevent recurrence of the hyperoxaluria induced damage in the transplanted kidney, the transplantation unit of University Hospitals Leuven elected to perform a combined kidney-intestinal transplantation. We present the two cases and highlight the underlying pathophysiological process of hyperoxaluria.

Notification:
This case has already been published in the American Journal of Transplantation in July 2013.
P 16
CASE REPORT

THYROID NODULES: RARE EVENTS OF METASTATIC INVASION OF RCC.

University Hospital Ghent, Ghent

Content:
Two patients are described, referred to our hospital for a nodule in the thyroid region.

- The first patient, a 67-year-old Caucasian man, presented with an enlarged left lobe with a solid mass with calcification and hypervascularisation. The nodule was confirmed on scintigraphy to be a cold nodule located in the inferior part of the left thyroid lobe. Fine needle aspiration was performed (FNA).

- The second patient, a 71-year-old Caucasian woman, which was in follow-up for a multinodular goiter, developed a suspect nodule in the right thyroid lobe with hypervascularisation on ultrasound (US). Two times FNA was performed.

In both patients, FNA revealed some atypical cells which demonstrated, on immunohistochemistry, expression of CK7, PAX8, CD10 and a negative reaction for TGB and TTF1. The diagnosis of a metastatic location of a renal cell carcinoma was suggested. In both cases, the clinical history did not mention the previous history of RCC. Eventually resection of the nodule was carried out with confirmation of the cytologic diagnosis. In the first patient, the RCC developed 19 years previously; the second patient developed the RCC 16 years priorly.

Review of the literature revealed that metastatic neoplasms to the thyroid gland are rare in clinical practice. CCRC is the most common primary tumor that metastasizes to the thyroid. [1] CCRC metastasizes in an unpredictable manner to organs and can show very late recurrence (up to 20 years). [2] When a patient with a history of cancer presents with a thyroid nodule, metastasis should always be excluded.


[2] Luca Foppiani, Michela Massollo, Patrizia Del Monte, Roberto Bandelloni, Anselmo Arlandini and Arnoldo Piccardo. Late-Onset Metastasis of Renal Cell Carcinoma into a Hot Thyroid Nodule: An Uncommon Finding Not to Be Overlooked. Case reports in Endocrinology 2015, Article ID 268714.
CASE REPORT

A CHALLENGING DIAGNOSIS FOR THE PATHOLOGIST: NUT MIDLINE CARCINOMA

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Content:

A 16-year old female has been referred to the hospital for severe cough and sore throat not responsive to antibiotics. Significant past medical history included myeloid acute leukaemia type 5 at the age of 6. Initial work up revealed a 9cm diameter solid mass centered on the right pulmonary hilum associated with multiple mediastinal and hilar lymphadenopathies. An endobronchial ultrasound (EBUS) has been carried out, leading to the diagnosis of blue cell tumour consisting in a poorly differentiated tumour composed of small cells with scant cytoplasm and round hyperchromatic nuclei forming sheets and nests. Tumour cells were focally positive for pan-keratin (AE1AE3) and negative for other epithelial markers (CK7, CK20, p63). Weak and focal expression of CD56 and NSE was observed, without any other neuroendocrine markers antigenicity (chromogranin, synaptophysin, CD57). There was a diffuse membranous expression of CD99. Mesenchymal and lymphoid markers were negative. Final diagnosis was in favour of Ewing/PNET Sarcoma family of tumours.

Nevertheless the EWSR1 translocation was not present, challenging this diagnosis. Clinicians decided to initiate treatment according to the 2008 Ewing protocol (vincristine, ifosfamide, doxorubicine, etoposide and radiotherapy). After eleven months the patient presented with motor aphasia and right hemipleagia. Brain MRI showed multiple supratentorial masses radiologically consistent with metastasis. Surgery was performed and pathological examination revealed a highly necrotic blue cell tumour. Immunohistochemical profile was identical to the thoracic tumour specimen. The cytogenetic analysis highlighted that the tumour exhibited highly altered karyotype in which was nevertheless identified a translocation between the long arm of chromosome 15 and the short arm of chromosome 19. This was confirmed by demonstration of a BRD4-NUT fusion transcript by RT-PCR resulting from the balanced translocation t (15; 19) (q14; p13.1).

This translocation is the hallmark of a recently recognised entity: NUT midline Carcinoma (NMC). In 1992 Kuzume and al. described the three first cases of thymic carcinoma with t(15,19) translocation. Since then enough cases have been collected to allow a proper clinicopathological description of the disease. NMC affects mainly young patients and arises in head, neck and mediastinum along the midline axis. It carries a dismal prognosis with a median overall survival of 6.7 months. NMC is a highly challenging diagnosis for pathologist since its morphological and immunohistochemical profile can mimic a wide range of disease. Misleading diagnosis included: sinonasal undifferentiated carcinoma, poorly differentiated squamous cell carcinoma, carcinosarcoma, thymic carcinoma and Ewing/PNET sarcoma family of tumour.
Since 2009, the resulting BRD4-NUT fusion protein nuclear overexpression is detectable by immunohistochemistry with sufficient sensitivity and specificity so that FISH assessment of t(15,19) translocation needs no longer to be performed.

Conventional chemotherapeutic agents are ineffective in treating NMC but nonetheless its unique genetic profile makes it a candidate for emerging targeted therapies, providing a strong rationale for accurate diagnosis of NMC by testing NUT expression in all midline poorly differentiated carcinoma.
P 18
EVALUATION OF SYNOPTIC PATHOLOGY REPORTING OF DUTCH COLORECTAL CARCINOMA


Introduction:

Traditional narrative pathology reporting (NR) can cause misinterpretation due to lack of information and structure. Therefore, in 2009, the Dutch Pathology Registry (PALGA) introduced synoptic reporting (SR) in the Netherlands initially for colorectal carcinoma (CRC) resections.

Aim:

This study investigated whether the completeness of CRC pathology reports and the quality of gross examination and pathology reports improved after introduction of SR.

Methods:

Pathology data of all CRC patients from 2007 up to 2013 was gathered using the Dutch Cancer Registry (data from NR and SR), and linked to data from PALGA (SR data). Completeness of a pathology report was defined as the proportion of pathology reports in which an individual parameter was present. Quality of CRC gross examination and PA reports was determined by evaluating the percentage of CRC resection specimens with ≥10 lymph nodes (LN) collected and the percentage of pathology reports describing a negative circumferential margin (CRM) respectively and compared between SR and NR (before and after the introduction of SR).

Results:

Data on 66189 CRC was collected, of which 29.6% were rectal carcinomas. 18139 tumours were reported narratively between 2007 and 2008, 28247 tumours were reported narratively between 2009 and 2013, and 19806 tumours were reported synoptically between 2009 and 2013.

Completeness: Before the introduction of SR, histological type, pT-stage, pN-stage and lymph nodes were already reported in more than 98% of the narrative reports. Histological grade and CRM were missing considerably more often, in 17.2% and 27.53% of the pathology reports respectively. With SR, a decrease in the proportion of pathology reports missing an individual parameter was observed for all parameters, especially for CRM, missing only in 2.0% of SR.
Quality: In the period after introduction of SR (2009 up to 2013), the percentage of CRC resection specimens with ≥10 LN collected was higher in SR (86.1%) than NR (75.7%) (p<0.001). Furthermore, for rectal carcinomas, a negative CRM was reported more often in SR (91.47%) than in NR before the introduction of SR (63.85%) and in NR after the introduction of SR (80.72%).

Conclusions:

SR appears to increase the probability that mandatory parameters are included in the pathology report, especially for CRM. Furthermore, it appears that the percentage of CRC resection specimens with ≥10 LNs collected increased at least partly due to SR. Additionally, SR seems to positively influence the reporting of CRM. Further analyses are necessary to study the effect of SR on quality of patient care.
P 19

TECHNICAL EVALUATION OF QVINTIP SELF-COLLECTED SAMPLES ON ABBOTT HIGH-RISK HPV AND AML QPCR HPV TEST.

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Introduction:

Since HPV testing is considered a valid method of choice for primary cervical cancer screening, the option for non-physician collected samples became a reachable alternative. Many countries, including Belgium, will exploit self-sampling to increase national screening coverage and aim to include hard-to-reach populations by a mail-based prevention approach. The recently introduced self-sampling device Qvintip (Aprovix AB, Sweden) has gained attention due to its limited size and excellent cell yield, and has hence to be considered as an important candidate self-sampling device for future outreach efforts. Qvintip collected samples are stored and shipped in the absence of any medium, prior to laboratory analysis.

Objective:

To evaluate the robustness of Qvintip self-sampling in combination with the AML qPCR HPV test and the Abbott high-risk HPV test.

Methods:

Samples were collected from 12 random female volunteers. Each woman was requested to collect two consecutive samples and carefully mark the order of collection. Collection was done according to the manufacturers information sheet, and no assistance was provided at the time of collection. Upon arrival at the laboratory, sample pairs were randomized into three different categories, and further incubated for 2-3 days. One sample of the pair was always kept at room temperature while the second sample was incubated either at 37°C (arm 1), at 4°C (arm 2), or at room temperature (arm 3). After incubation, DNA was extracted according to Abbott M2000sp specifications, and analyzed with both HR HPV tests (Abbott and AML qPCR).

Results:

Valid results were obtained from all samples, and using both tests. The Abbott test gave an average Cq=20.30 and the AML qPCR Cq=23.26 for beta-Globin. The overall quantitative difference in the beta-Globin Cq between the first collected and the consecutive sample was ΔCq=0.31 (Abbott) and ΔCq=0.32 (AML). The influence of temperature was limited; incubation at 4°C induced a difference in beta-Globin of ΔCq=0.07 (Abbott) and ΔCq=0.20 (AML) and incubation at 37°C of ΔCq=0.65 (Abbott) and ΔCq=0.77 (AML) between paired samples.
Only one sample out of 12 tested positive for HPV, being a triple infection with HPV 35, HPV 59 and HPV 66. No discrepancies were found between the first and second sample at qualitative level for both Abbott and AML test (for AML also at full genotyping level), and only non-significant variation at quantitative level could be noted.

**Discussion:**

Our preliminary findings suggest that the combination of Qvintip-based self-collected samples and Abbott HR HPV test or AML qPCR test renders a robust configuration. The data also suggest that collection of two consecutive samples is possible without significant loss of DNA content. Furthermore, our data suggest that the temperature at which the self-sampling device is kept, did not induce a significant difference.