

Traceability and treatment of cervical cancer patients in the High-Energy Radiotherapy Laboratory

Trasabilitatea și tratamentul pacienților cu cancer de col uterin în cadrul Laboratorului de radioterapie cu energii înalte

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Introduction. Cervical cancer is among the most common cancers afflicting women worldwide. This paper presents all stages of preparation, scanning, radiotherapy treatment planning and verification for patients diagnosed with malignant cervical cancer and treatment delivery. Two types of treatment using ionizing radiation are presented and evaluated, external beam radiotherapy EBRT (photon) and three-dimensional intracavitary high-dose rate (3D-HDR) closed source Iridium 192 brachytherapy. The treatment planning, optimization and quality assurance are the precursor steps to quality assurance activities of radiological facilities and training of laboratory staff by medical physicists. **Materials used in radiotherapy treatment.** External: CT simulator (dedicated tomographic computer for obtaining the images necessary for external treatment planning), special means of patient restraint (foot support, knee support, mattresses), radiopaque markers, head brace type support, monoenergetic medical linear accelerator (Elekta Infinity – photon beam) or with dual energy (True Beam – photon beams), 6 MV and 15 MV, systems for ensuring the quality of treatment plans (ArcCHECK phantom, manufacturer Sun Nuclear and electronic portal imaging device EPID, manufacturer Varian Medical Systems), positioning lasers, stylus, syringes, injectors, contrast substance for better visualization in the contouring stage, dosimetric equipment for checking the quality of radiological equipment, video camera and microphone. Intracavitary: CT simulator (dedicated tomographic computer for rendering the images necessary for external treatment planning), Gamma Med Plus type brachytherapy installation, manufacturer Varian Medical Systems, special portable brachytherapy table, intracavitary applicators, radiopaque markers for applicators, gynecological measuring equipment of patients' hysteroscopy, forceps, syringes, bladder probe, tables, wires for source transfer. Equipment for checking the position of the source, part of quality assurance, dosimetric equipment such as radiation detectors, video camera and microphone. External beam radiation therapy (EBRT) is a standard cancer treatment and the most common form of radiation therapy. It uses a machine to send energy beams that destroy tumors. EBRT relies on advanced technology that designs radiation treatments to destroy cancer cells while reducing damage to surrounding healthy tis-

sue. It is a local treatment, which means it treats a specific part of the body. Most radiotherapy machines use photon beams. Photon beams can reach tumors deep in the body. Brachytherapy (BT) is a treatment technique that uses enclosed radiation sources (Ir-192) to deliver a radiation dose directly to the planned target volume (PTV). It allows a precise delimitation of the target and the volumes of the organs at risk. Consequently, local recurrences were reduced, and the survival rates were improved. Using a linear-quadratic model, cumulative doses of external beam radiotherapy and 3D-IGRT were summed and normalized to a biologically equivalent dose of 2 Gy per fraction (EQD2). Treatment planning in high-dose rate (HDR) brachytherapy based on three-dimensional (3D) imaging enables the pre-arrangement and optimal treatment. This process consists of planning the procedure, choosing applicators, adjusting the appropriate implantation technique, and planning the three-dimensional dose distribution in the computerized treatment planning system. The 3D images used in HDR brachytherapy treatment planning allow for choosing the most appropriate application technique. **Conclusions.** The treatment of this disease is represented by radiochemotherapy, external RT, followed by brachytherapy and, in certain cases, the surgical treatment. Radiochemotherapy and intracavitary brachytherapy are indicated in early, small-volume, low-grade tumors. 3D HDR brachytherapy allows the best coverage of the area by the reference dose with simultaneous protection of critical organs. The treatment planning on 3D images ensures individual planning of dose dispersion in the target area. ArcCHECK is an array of detectors specifically designed to identify errors in rotary delivery. It is the ideal solution for pre-treatment patient QA in IMRT and VMAT techniques, including specialty systems such as Varian Medical Systems or Elekta. EPID has two major advantages: EPID is integrated with the LINAC portal, and the QA procedure can be set up faster. Secondly, EPID data are digital, which greatly facilitates data post-processing, transfer, analysis and storage. A multidisciplinary team of specialists and medical assistants is involved in all stages of treatment. Preoperative or postoperative radiochemotherapy combined treatments have a different approach from the point of view of the radiation therapist and the medical physicist.

Keywords: cervical cancers, radiotherapy

Risk of pancreatic fistula after pancreatoduodenectomy – a point of view *Riscul de fistulă pancreatică după pancreatoduodenectomie – un punct de vedere*

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Cephalic pancreatoduodenectomy, a complex and difficult surgical procedure, has as main indication the radical treatment of pancreatic head cancers, but is also used in other periampullary tumors (neoplasms of the terminal choledochus, duodenal tumors, Vaterian ampulloma, GIST). If the resection part of this procedure is well standardized, the reconstruction part has many variants, the most frequently used being the Whipple procedure, which involves restoring alimentary, bile and pancreatic transit in series on a jejunal loop. During the almost 100 years since this surgery has been practiced, the postoperative results have improved spectacularly, except for an increased incidence of pancreatic fistula, which can vary from 6% in centers of excellence to 30% in other centers. It is actually a complex, polluted, ali-

mentary and biliary fistula, associated with high morbidity and mortality, reaching up to 26%. It is not the surgical technique but the quality of the pancreatic partner of this anastomosis that makes it being considered the "Achilles heel" of this operation. The authors, after evaluating various methods of pancreatic-digestive derivations, propose the way with elements of originality to achieve pancreatic-jejunal anastomosis (on isolated loop "à la Roux" axially drained uniquely, both biliary and pancreatic) that can decrease the incidence of fistula and diminish its severity, improving morbidity and mortality through this postoperative complication.

Keywords: pancreatic fistula, pancreatic-jejunal anastomosis on isolated loop, cephalic pancreatoduodenectomy, axial drainage

Assessment of genomic alterations in colorectal cancer using a targeted multigene panel next-generation sequencing – preliminary results

Evaluarea alterărilor genetice în cancerul colorectal prin secvențiere de nouă generație utilizând un panel multigenic țintit – rezultate preliminare

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Introduction. In Romania, colorectal cancer (CRC) represents the second cause of tumor mortality due to cancer. DNA profiles can guide the clinical management and provide valuable information regarding the diagnosis, prognosis and treatment guidelines. Next-generation sequencing (NGS) is a technology that allows the simultaneous evaluation of many genes, and it is increasingly used in clinical practice. **Objective.** The aim of this study was to describe the mutations landscape of CRC using NGS technology. **Materials and method.** DNA was manually extracted from fresh tumor samples collected from 76 patients using QIAmp DNA Mini kit (Qiagen). Multiplex PCR libraries were obtained from 12 ng of DNA with Ion AmpliSeq Library Kit 2.0. NGS was performed with Ion AmpliSeq Cancer Hotspot Panel v2. Clonal amplification and enrichment were done with the Ion OneTouch 2 System. The sequencing was done on the Ion Personal Genome Machine (PGM) and Ion 316 Chip v2 (ThermoFisher Scientific). The analyses were performed with Torrent Suite Software v5.2.1, Ion Reporter Software 5.10 (ThermoFisher Scientific), Integrative Genomics Viewer and COSMIC database. The following filtering

parameters were used: variant frequency >5%, average coverage depth >100x, variant coverage >20x, p value <0.01, and bidirectional reads. **Results.** In this study, 77.6% of the tumors were located in the left colon, similar to data from literature. Mutations were identified in 26 of the total of 50 genes (50.2%) covered by the kit. There were detected 130 different alterations; 38.5% (50/130) were pathogenic, 3.1% (4/130) were likely pathogenic, and 14.6% (19/130) were not reported in COSMIC. The rest of the mutations has no indication regarding the clinical impact. The most frequent mutated genes were APC (63.2%), TP53 (61.8%), KRAS (51.3%), PIK3CA (19.7%), BRAF (14.5%), and SMAD4 (10.5%). Several samples had multiple mutations at the same genes. **Conclusions.** Mainly, the multiple mutations affecting the same gene were pathogenic and were identified in patients with the advanced stage of the disease (pT3) and with tumor localization in the rectum. Due to the large volume of data to analyze, the presented results are preliminary, and the follow-up of the patients' evolution is in progress.

Keywords: colorectal cancer, next-generation sequencing, Ion Personal Genome Machine

Operative standards in sarcomas of extremities *Standarde operative în sarcoamele extremităților*

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Sarcomas are solid, malignant tumors of mesenchymal origin, having a high heterogeneity, with more than 100 different histological subtypes. Although rare, with an incidence of about 1% of adult neoplasms, they frequently have aggressive forms, with a more reserved prognosis compared to other more common cancers. The higher incidence, around 40%, is found in the upper and lower limbs. Creating a "high-volume" center of excellence to focus on this pathology is a logical decision to improve the outcomes and optimize resource utilization. The use of treatment standards, including surgical evidence-based ones, is a must. Decisions are made in a mandatory tumor board that includes at least one sarcoma expert. Preoperatively imaging evaluation (MRI) and biopsy – preferably the core-needle biopsy variant – are indispensable. Surgical resection with or without neoadjuvant treatment is the

main therapeutic approach in non-metastasized forms. The resection is done *en bloc* with the biopsy tract, and must include a safety limit of at least 2 cm and, also, with uninvaded surgical margins (R0). The type of intervention is individualized to each patient, depending on the histopathological form, size and location of the tumor, ranging from extracompartmental resections to wide or marginal excision. Amputation should be avoided, if possible, because it does not bring benefits in terms of survival. Lymphadenectomy is rarely necessary, and it has a prognostic value. Clipping the tumor bed or, possibly, the residual tumor is useful for adjuvant radiation therapy. Surgical suction drainage is done routinely to avoid hematomas or postoperative seromas.

Keywords: sarcoma of extremities, operative standards, preoperative biopsy, R0 resection

Identification of potential errors in tumor marker daily routine testing using external quality control in the medical laboratories

Identificarea erorilor care pot apărea în testarea zilnică a markerilor tumorali folosind controlul extern al calității în laboratoarele medicale

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Objective. External quality control (EQC) schemes are crucial in identifying potential errors, discrepancies and variations in tumor marker testing methodologies. This study aims to evaluate the performance of medical laboratories in Romania participating in the EQC schemes carried out in 2023. The focus is the testing of tumor markers such as total and free prostate-specific antigen (PSA and free PSA), carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9), 15-3 (CA 15-3) and 125 (CA 125), and identifying the possible causes of the reported systematic and random errors. **Materials and method.** The study used data from an EQC provider, representing results reported by 713 medical laboratories in six rounds during 2023. The performance of the laboratories participating in EQC schemes was evaluated using statistical calculations, such as assigned value, D, D%, CV, acceptability range, and Z or Z' score. The results were presented as mean ± standard deviation (SD). **Results.** The average of unsatisfactory results for

the six rounds (March, April, May, September, October, November) in 2023 was as follows: PSA (2.48±0.16%), free PSA (3.77±0.20%), CA 19-9 (2.12±0.12%), CA 15-3 (5±0.63%), CA 125 (3.38±0.20%), and CEA (2.72±0.12%). The main errors identified are due to the incorrect reconstruction of the object subject to the proficiency test, failure to comply with the results reporting procedure, misreporting EQC results, misuse of conversion factors, and the wrong choice of the comparison group for the reported data. **Conclusions.** The study's results indicated that the EQC schemes had an average satisfactory result rate of over 95% for testing the selected tumor markers. The percentage of unsatisfactory results ranged from 2.12% to 5% on average in 2023, suggesting a high level of accuracy in tumor marker testing. These findings pave the way for further improvements in quality control and testing methodologies.

Keywords: external quality control schemes, tumor marker testing, medical laboratories performance

HER2 genotype and tumor cells proliferation in urinary bladder cancer Genotipul HER2 și proliferarea celulelor tumorale în cancerul de vezică urinară

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HER2 gene, located in chromosome 17q12–q21, encodes a transmembrane protein of 185 kDa with tyrosine kinase activity and an important role in tumorigenesis. The presence of the Ile655Val polymorphism identified in transmembrane domain of the HER2 protein was observed in tumors with different locations. Previous studies have shown that changing the existing isoleucine (Ile) to valine (Val) at codon 655 of the HER2 gene causes an intensification of dimerization, autophosphorylation of the HER2 receptor, as well as tyrosine kinase activity, which influences cell growth and tumor proliferation. The aim of this study was to assess the HER2 codon 655 polymorphism related to tumor cells proliferation in urinary bladder cancer. Tumors obtained from patients with bladder cancer were analyzed by PCR-RFLP for the presence of polymorphism at codon 655 of the HER2 gene. The expression of HER2 and pHER2 proteins was

determined immunohistochemically. The DNA content, from the tumor cells, was analyzed by flow cytometry for cell cycle phases and DNA ploidy. HER2 heterozygous genotype was dominant in carcinomas with co-expression of HER2 and pHER2. The tumors HER2 and pHER2 positive from Ile/Val genotype group had a higher level of S-phase fraction than those from Ile/Ile genotype group. The S-phase fraction was also elevated in heterozygous than homozygous tumor in patients with lymph node metastases. The HER2 heterozygous cases were aneuploid predominantly. The presence of Ile/Val genotype in bladder carcinoma seems to be associated with a high proliferation. These results may suggest that HER2 codon 655 polymorphism can be used in the evaluation of disease progression in bladder cancer.

Keywords: HER2 genotype, S-phase fraction, bladder carcinoma

Dynamics of radioactive iodine blood concentration following therapy in patients with differentiated thyroid cancer

Dinamica concentrației sanguine de iod radioactiv la pacienții cu cancer tiroidian diferențiat

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Objective. We hypothesized that patients with differentiated thyroid (DTC) cancer and higher tumor burden may exhibit prolonged release of radioactive iodine (¹³¹I) into the bloodstream following therapy. The study aimed to investigate the temporal pattern of ¹³¹I blood concentration post-intake. **Materials and method.** Fifty female patients, with a mean age of 58.98±10.85 years old, who received a ¹³¹I median activity of 90.54 mCi (3.35 GBq), were enrolled in the study. Whole-body dose rate and whole-blood radioactivity measurements were conducted at different time intervals (6, 22, 46, 69 and 92 hours) after administering the ¹³¹I therapeutic dose. **Results.** The results revealed a biphasic pattern of ¹³¹I blood concentration, with peaks observed at 46 and 69 hours after intake. Whole-blood radioactivity decreased within the first 46 hours, but increased at the 69-hour mark, suggesting a dynamic process of uptake and clearance of ¹³¹I from the bloodstream. Moreover, ¹³¹I activity correlated with whole-blood radioactiv-

ity at both 69 hours (r=0.509; p<0.001) and 92 hours (r=0.488; p<0.001). The significant positive correlation indicates that ¹³¹I remains in the blood circulation in a high percentage even after 92 hours. The slight decrease of the correlation coefficient from 69 to 92 hours shows that, after this interval, slow elimination of ¹³¹I from the blood circulation occurs. **Conclusions.** The first peak measured at 46 hours corresponds to the peak uptake of ¹³¹I in residual thyroid tissue, indicating the efficacy of therapy in targeting thyroid cancer cells. The subsequent peak at 69 hours suggests a secondary phase of response, possibly involving the release of inflammatory mediators. Understanding the temporal pattern of ¹³¹I blood concentration can aid clinicians in optimizing treatment protocols and in assessing the therapeutic efficacy regarding the optimal ¹³¹I dose to be administered.

Keywords: radioactive iodine therapy, whole-blood radioactivity, differentiated thyroid cancer