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Índice

J Nucl Med. 2016 Feb;57 Suppl 1:69S-74S.

Novel Strategies for Breast Cancer Imaging: New Imaging Agents to Guide Treatment.

McDonald ES, Mankoff DA, Mach RH.

The development of molecular therapies for cancer treatment has created a need to image biochemical and molecular processes to appropriately select tumors that express the drug target, thereby predicting a positive response to therapy. Biomarker-driven molecular imaging is complementary to pathologic analysis and offers a more direct measure of drug efficacy and treatment response, potentially providing early insight into therapeutic futility and allowing response-adapted treatment strategies. Imaging also allows a unique means of assessing the heterogeneity of both intra- and intertumoral targets as well as a mixed response to therapy; this information is important in the setting of metastatic disease. Here we review the development of novel molecular imaging probes and combinations of probes to guide therapy for two new targets and associated therapeutic agents: cyclin-dependent kinase inhibitors and poly(adenosine diphosphate-ribose) polymerase inhibitors.

PMID: 26834105 [PubMed - indexed for MEDLINE]

Eur J Radiol. 2016 Jan;85(1):113-24

Diffusion volume (DV) measurement in endometrial and cervical cancer: A new MRI parameter in the evaluation of the tumor grading and the risk classification.

Mainenti PP, Pizzuti LM, Segreto S, Comerci M, Fronzo SD, Romano F, Crisci V, Smaldone M, Laccetti E, Storto G, Alfano B, Maurea S, Salvatore M, Pace L.

PURPOSE: A new MRI parameter representative of active tumor burden is proposed: diffusion volume (DV), defined as the sum of all the voxels within a tumor with apparent diffusion

coefficient (ADC) values within a specific range. The aims of the study were: (a) to calculate DV on ADC maps in patients with cervical/endometrial cancer; (b) to correlate DV with histological grade (G) and risk classification; (c) to evaluate intra/inter-observer agreement of DV calculation. MATERIALS AND METHODS: Fifty-three patients with endometrial (n=28) and cervical (n=25) cancers underwent pelvic MRI with DWI sequences. Both endometrial and cervical tumors were classified on the basis of G (G1/G2/G3) and FIGO staging (low/medium/high-risk). A semi-automated segmentation procedure was used to calculate the DV. A freehand closed ROI outlined the whole visible tumor on the most representative slice of ADC maps defined as the slice with the maximum diameter of the solid neoplastic component. Successively, two thresholds were generated on the basis of the mean and standard deviation (SD) of the ADC values: lower threshold (LT="mean minus three SD") and higher threshold (HT="mean plus one SD"). The closed ROI was expanded in 3D, including all the contiguous voxels with ADC values in the range LT-HT × 10-3mm(2)/s. A Kruskal-Wallis test was used to assess the differences in DV among G and risk groups. Intra-/inter-observer variability for DV measurement was analyzed according to the method of Bland and Altman and the intraclass-correlation-coefficient (ICC). RESULTS: DV values were significantly different among G and risk groups in both endometrial ($p<0.05$) and cervical cancers ($p \leq 0.01$). For endometrial cancer, DV of G1 (mean ± sd: 2.81 ± 3.21 cc) neoplasms were significantly lower than G2 (9.44 ± 9.58 cc) and G3 (11.96 ± 8.0 cc) ones; moreover, DV of low risk cancers (5.23 ± 8.0 cc) were significantly lower than medium (7.28 ± 4.3 cc) and high risk (14.7 ± 9.9 cc) ones. For cervical cancer, DV of G1 (0.31 ± 0.13 cc) neoplasms was significantly lower than G3 (40.68 ± 45.65 cc) ones; moreover, DV of low risk neoplasms (6.98 ± 8.08 cc) was significantly lower than medium (21.7 ± 17.13 cc) and high risk (62.9 ± 51.12 cc) ones and DV of medium risk neoplasms was significantly lower than high risk ones. The intra-/inter-observer variability for DV measurement showed an excellent correlation for both cancers (ICC ≥ 0.86). CONCLUSIONS: DV is an accurate index for the assessment of G and risk classification of cervical/endometrial cancers with low intra-/inter-observer variability.

PMID: 26724655 [PubMed - indexed for MEDLINE]

Drug Discov Ther. 2015 Oct;9(5):310-8.

Hepatocellular carcinoma: Advances in diagnostic imaging.

Sun H, Song T.

Thanks to the growing knowledge on biological behaviors of hepatocellular carcinomas (HCC), as well as continuous improvement in imaging techniques and experienced interpretation of

imaging features of the nodules in cirrhotic liver, the detection and characterization of HCC has improved in the past decade. A number of practice guidelines for imaging diagnosis have been developed to reduce interpretation variability and standardize management of HCC, and they are constantly updated with advances in imaging techniques and evidence based data from clinical series. In this article, we strive to review the imaging techniques and the characteristic features of hepatocellular carcinoma associated with cirrhotic liver, with emphasis on the diagnostic value of advanced magnetic resonance imaging (MRI) techniques and utilization of hepatocyte-specific MRI contrast agents. We also briefly describe the concept of liver imaging reporting and data systems and discuss the consensus and controversy of major practice guidelines.

PMID: 26632539 [PubMed - indexed for MEDLINE]

Mo Med. 2015 Sep-Oct;112(5):373-8.

Imaging Advances in Stereotactic Radiosurgery.

Tsien C, Drzymala RE, Rich K.

Novel functional and metabolic MRI imaging provides the ability to analyze tumor tissue properties including tumor vasculature, vascular permeability, tumor cellularity, hypoxia, and tumor proliferation. Stereotactic radiosurgery involves the delivery of a very precise, focal dose of radiation to a target. Recent advances in MR imaging have the potential to improve accuracy for target volume delineation and to potentially improve outcome. Novel MR imaging techniques may also be used in subsequent post-treatment follow-up to distinguish between tumor recurrences versus non-neoplastic treatment-related changes. In this paper, we address multiparametric MR imaging and cerebral angiography as tools to reduce toxicity.

PMID: 26606819 [PubMed - indexed for MEDLINE]

Pancreas. 2015 Nov;44(8):1185-94.

Advances in Biomedical Imaging, Bioengineering, and Related Technologies for the evelopment of Biomarkers of Pancreatic Disease: Summary of a National Institute of Diabetes and Digestive and Kidney Diseases and National Institute of Biomedical Imaging and Bioengineering Workshop.

Kelly KA, Hollingsworth MA, Brand RE, Liu CH, Singh VK, Srivastava S, Wasan AD, Yadav D, Andersen DK.

A workshop sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute of Biomedical Imaging and Bioengineering focused on research gaps and opportunities in the development of new biomarkers of pancreatic disease. The session was held on July 22, 2015, and structured into 6 sessions: 1) Introduction and Overview; 2) Keynote Address; 3) New Approaches to the Diagnosis of Chronic Pancreatitis; 4) Biomarkers of Pain and Inflammation; 5) New Approaches to the Detection of Pancreatic Cancer; and 6) Shed Exosomes, Shed Cells, and Shed Proteins. Recent advances in the fields of pancreatic imaging, functional markers of pancreatic disease, proteomics, molecular and cellular imaging, and detection of circulating cancer cells and exosomes were reviewed. Knowledge gaps and research needs were highlighted. The development of new methods for the noninvasive determination of pancreatic pathology; the use of cellular markers of pancreatic function, inflammation, pain, and malignancy; and the refinement of methods to identify cells and cellular constituents of pancreatic cancer were discussed. The further refinement of sophisticated technical methods and the need for clinical studies to validate these new approaches in large-scale studies of patients at risk for the development of pancreatic disease were repeatedly emphasized.

PMCID: PMC4608388 [Available on 2016-11-01]
PMID: 26465948 [PubMed - indexed for MEDLINE]

Nat Rev Urol. 2015 Aug;12(8):435-44.

Addressing the need for repeat prostate biopsy: new technology and approaches.

Blute ML Jr, Abel EJ, Downs TM, Kelcz F, Jarrard DF.

No guidelines currently exist that address the need for rebiopsy in patients with a negative diagnosis of prostate cancer on initial biopsy sample analysis. Accurate diagnosis of prostate cancer in these patients is often complicated by continued elevation of serum PSA levels that are suggestive of prostate cancer, resulting in a distinct management challenge. Following

negative initial findings of biopsy sample analysis, total serum PSA levels and serum PSA kinetics are ineffective indicators of a need for a repeat biopsy; therefore, patients suspected of having prostate cancer might undergo several unnecessary biopsy procedures. Several alternative strategies exist for identifying men who might be at risk of prostate cancer despite negative findings of biopsy sample analysis. Use of other serum PSA-related measurements enables more sensitive and specific diagnosis and can be combined with knowledge of clinicopathological features to improve outcomes. Other options include the FDA-approved Progensa(®) test and prostate imaging using MRI. Newer tissue-based assays that measure methylation changes in normal prostate tissue are currently being developed. A cost-effective strategy is proposed in order to address this challenging clinical scenario, and potential directions of future studies in this area are also described.

PMID: 26171803 [PubMed - indexed for MEDLINE]

AJR Am J Roentgenol. 2015 Jul;205(1):W42-55.

MRI of Rectal Cancer: An Overview and Update on Recent Advances.

Jhaveri KS, Hosseini-Nik H.

OBJECTIVE: MRI is the modality of choice for rectal cancer staging. The high soft-tissue contrast of MRI accurately assesses the extramural tumor spread and relation to mesorectal fascia and the sphincter complex. This article reviews the role of MRI in the staging and treatment of rectal cancer. The relevant anatomy, MRI techniques, preoperative staging, post-chemoradiation therapy (CRT) imaging, and tumor recurrence are discussed with special attention to recent advances in knowledge. CONCLUSION: MRI is the modality of choice for staging rectal cancer to assist surgeons in obtaining negative surgical margins. MRI facilitates the accurate assessment of mesorectal fascia and the sphincter complex for surgical planning. Multiparametric MRI may also help in the prediction and estimation of response to treatment and in the detection of recurrent disease.

PMID: 26102418 [PubMed - indexed for MEDLINE]

Med Ultrason. 2015 Jun;17(2):227-34.

Endoscopic ultrasound for the characterization and staging of rectal cancer. Current state of the method. Technological advances and perspectives.

Gersak MM, Badea R, Graur F, Hajja NA, Furcea L, Dudea SM.

Endoscopic ultrasound is the most accurate type of examination for the assessment of rectal tumors. Over the years, the method has advanced from gray-scale examination to intravenous contrast media administration and to different types of elastography. The multimodal approach of tumors (transrectal, transvaginal) is adapted to each case. 3D ultrasound is useful for spatial representation and precise measurement of tumor formations, using CT/MR image reconstruction; color elastography is useful for tumor characterization and staging; endoscopic ultrasound using intravenous contrast agents can help study the amount of contrast agent targeted at the level of the tumor formations and contrast wash-in/wash-out time, based on the curves displayed on the device. The transvaginal approach often allows better visualization of the tumor than the transrectal approach. Performing the procedure with the rectal ampulla distended with contrast agent may be seen as an optimization of the examination methodology. All these aspects are additional methods for gray-scale endoscopic ultrasound, capable of increasing diagnostic accuracy. This paper aims at reviewing the progress of transrectal and transvaginal ultrasound, generically called endoscopic ultrasound, for rectal tumor diagnosis and staging, with emphasis on the current state of the method and its development trends.

PMID: 26052575 [PubMed - indexed for MEDLINE]

Semin Radiat Oncol. 2015 Jul;25(3):164-71

Advances in Magnetic Resonance Imaging and Positron Emission Tomography Imaging for Grading and Molecular Characterization of Glioma.

Chung C, Metser U, Ménard C.

In recent years, the management of glioma has evolved significantly, reflecting our better understanding of the underlying mechanisms of tumor development, tumor progression, and treatment response. Glioma grade, along with a number of underlying molecular and genetic biomarkers, has been recognized as an important prognostic and predictive factor that can help guide the management of patients. This article highlights advances in magnetic resonance imaging (MRI), including diffusion-weighted imaging, diffusion tensor imaging, magnetic resonance spectroscopy, dynamic contrast-enhanced imaging, and perfusion MRI, as well as position emission tomography using various tracers including methyl-(11)C-l-methionine and O-

(2-(18)F-fluoroethyl)-l-tyrosine. Use of multiparametric imaging data has improved the diagnostic strength of imaging, introduced the potential to noninvasively interrogate underlying molecular features of low-grade glioma and to guide local therapies such as surgery and radiotherapy.

PMID: 26050586 [PubMed - indexed for MEDLINE]

Clin Oncol (R Coll Radiol). 2015 Sep;27(9):495-7.

Magnetic Resonance Imaging-guided Radiation Therapy: Technological Innovation Provides a New Vision of Radiation Oncology Practice.

Oelfke U.

PMID: 25960321 [PubMed - indexed for MEDLINE]

Urol Clin North Am. 2015 May;42(2):147-57, vii.

Advances in imaging technologies in the evaluation of high-grade bladder cancer.

Zlatev DV, Altobelli E, Liao JC.

Bladder cancer ranges from a low-grade variant to high-grade disease. Assessment for treatment depends on white light cystoscopy, however because of its limitations there is a need for improved visualization of flat, multifocal, high-grade, and muscle-invasive lesions. Photodynamic diagnosis and narrow-band imaging provide additional contrast enhancement of bladder tumors and have been shown to improve detection rates. Confocal laser endomicroscopy and optical coherence tomography enable real-time, high-resolution, subsurface tissue characterization with spatial resolutions similar to histology. Molecular imaging offers the potential for the combination of optical imaging technologies with cancer-specific molecular agents to improve the specificity of disease detection.

PMCID: PMC4402158
PMID: 25882557 [PubMed - indexed for MEDLINE]

Clin Mol Hepatol. 2015 Mar;21(1):95-103.

Recent advances in the imaging of hepatocellular carcinoma.

You MW, Kim SY, Kim KW, Lee SJ, Shin YM, Kim JH, Lee MG.

The role of imaging is crucial for the surveillance, diagnosis, staging and treatment monitoring of hepatocellular carcinoma (HCC). Over the past few years, considerable technical advances were made in imaging of HCCs. New imaging technology, however, has introduced new challenges in our clinical practice. In this article, the current status of clinical imaging techniques for HCC is addressed. The diagnostic performance of imaging techniques in the context of recent clinical guidelines is also presented.

PMCID: PMC4379204
PMID: 25834808 [PubMed - indexed for MEDLINE]

Curr Opin Oncol. 2015 May;27(3):224-31.

Advances in imaging modalities in prostate cancer.

Bouchelouche K, Turkbey B, Choyke PL.

PURPOSE OF REVIEW: Imaging plays an important role in the clinical management of prostate cancer (PCa). Thus, much effort has gone into improving imaging modalities in PCa. This review focuses on the recent advancements in transrectal ultrasound, MRI and PET during the past year. RECENT FINDINGS: Contrast-enhanced transrectal ultrasound with microbubbles may be useful in PCa, but needs further evaluation before more widespread use. Multiparametric MRI has emerged as a valuable tool to assist clinical management of PCa, and great progress has been made in the past year. Several radionuclides for PET/computed tomography have been tested in clinical trials; most of the studies have used radiolabeled choline. However, new PET tracers such as (18)F-1-amino-3-fluorine 18-fluorocyclobutane-1-carboxylic acid and (68)Ga-labeled prostate-specific membrane antigen ligands are demonstrating promising results. PET/MRI may further improve imaging in PCa, but this imaging modality needs to be evaluated further. SUMMARY: Several advances in the imaging of PCa have been made during the past year. In particular, important clinical developments have been reported in multiparametric MRI, PET/computed tomography, and PET/MRI. The continuing development of imaging techniques in PCa has the potential to optimize treatment of PCa. However, the optimal imaging strategies for each of the major clinical scenarios in PCa have not yet been identified.

PMID: 25715326 [PubMed - indexed for MEDLINE]

Curr Opin Urol. 2015 May;25(3):191-7.

Ultrasound modalities and quantification: developments of multiparametric ultrasonography, a new modality to detect, localize and target prostatic tumors.

Postema A(1), Idzenga T, Mischi M, Frinking P, de la Rosette J, Wijkstra H.

PURPOSE OF REVIEW: An imaging tool providing reliable prostate cancer (PCa) detection and localization is necessary to improve the diagnostic pathway with imaging targeted biopsies. This review presents the latest developments in existing and novel ultrasound modalities for the detection and localization of PCa. RECENT FINDINGS: The ultrasound modalities that were very promising on introduction (HistoScanning and Doppler) have shown a wane in performance when tested in larger patient populations. In the meantime, novel ultrasound modalities have emerged in the field of PCa detection. Modalities, such as shear wave elastography (SWE) and contrast-enhanced ultrasound (CEUS) show very promising results. SWE produces an absolute elasticity measure and removes the need for manual compression of the tissue. The former allows comparison between scans and patients, the latter reduces the interoperator variability. Quantification of CEUS enables easily interpretable and accurate imaging of the microvascular changes associated with clinically significant prostate tumors. SUMMARY: The novel ultrasound modalities of SWE and CEUS imaging open the door for taking targeted biopsies based on the detection and localization of PCa by these novel modalities. This potentially improves PCa detection wherein significantly reducing the number of biopsy cores.

PMID: 25695792 [PubMed - indexed for MEDLINE]

J Hepatol. 2015 Mar;62(3):690-700.

New imaging techniques for liver diseases.

Van Beers BE, Daire JL, Garteiser P.

Comment in

J Hepatol. 2015 Aug;63(2):535.

J Hepatol. 2015 Aug;63(2):534.

Newly developed or advanced methods of ultrasonography and MR imaging provide combined anatomical and quantitative functional information about diffuse and focal liver diseases. Ultrasound elastography has a central role for staging liver fibrosis and an increasing role in grading portal hypertension; dynamic contrast-enhanced ultrasonography may improve tumor characterization. In clinical practice, MR imaging examinations currently include diffusion-weighted and dynamic MR imaging, enhanced with extracellular or hepatobiliary contrast agents.Moreover, quantitative parameters obtained with diffusion-weighted MR imaging, dynamic contrast-enhanced MR imaging and MR elastography have the potential to characterize further diffuse and focal liver diseases, by adding information about tissue cellularity, perfusion, hepatocyte transport function and visco-elasticity. The multiparametric capability of ultrasonography and more markedly of MR imaging gives the opportunity for high diagnostic performance by combining imaging biomarkers. However, image acquisition and post-processing methods should be further standardized and validated in multicenter trials.

PMID: 25457198 [PubMed - indexed for MEDLINE]

Curr Opin Gastroenterol. 2015 Jan;31(1):76-80.

Recent developments in colorectal imaging.

Pickhardt PJ

PURPOSE OF REVIEW: The aim of this review is to provide an update on important recent advances in radiologic colorectal imaging, with emphasis on detection, staging, and surveillance of colorectal neoplasia. RECENT FINDINGS: Colorectal imaging advances with magnetic resonance (MR), computed tomography colonography (CTC), and positron emission tomography (PET) over the past year or so have been substantial. Progress in MRI for rectal cancer was most notable in terms of assessment of response to neoadjuvant therapy. Continued maturation and clinical validation of CTC was observed for the evaluation of advanced neoplasia, among other areas. Multimodality approaches to colorectal imaging that incorporate functional PET data have also made impressive strides forward. SUMMARY: Recent advances in cross-sectional and functional radiologic imaging of the colorectum will positively impact the clinical capabilities for noninvasive evaluation of colorectal neoplasia.

PMCID: PMC4278653 . PMID: 25394232 [PubMed - indexed for MEDLINE]

Science. 2016 Jun 17;352(6292):1417-20.

From the RNA world to the clinic.

Sullenger BA, Nair S.

The study of RNA has continually emphasized the structural and functional versatility of RNA molecules. This versatility has inspired translational and clinical researchers to explore the utility of RNA-based therapeutic agents for a wide variety of medical applications. Several RNA therapeutics, with diverse modes of action, are being evaluated in large late-stage clinical trials, and many more are in early clinical development. Hundreds of patients are enrolled in large trials testing messenger RNAs to combat cancer, small interfering RNAs to treat renal and hepatic disorders, and aptamers to combat ocular and cardiovascular disease. Results from these studies are generating considerable interest among the biomedical community and the public and will be important for the future development of this emerging class of therapeutic agents.

PMID: 27313039 [PubMed - indexed for MEDLINE]

Nature. 2016 Jun 1;534(7607):329-31.

Immunotherapy: Cancer vaccine triggers antiviral-type defences.

De Vries J, Figdor C.

Comment on
Nature. 2016 Jun 16;534(7607):396-401.

PMID: 27281206 [PubMed - indexed for MEDLINE]

Nature. 2016 Jun 1;534(7607):396-401.

Systemic RNA delivery to dendritic cells exploits antiviral defence for cancer immunotherapy.

Kranz LM, Diken M, Haas H, Kreiter S, Loquai C, Reuter KC, Meng M, Fritz D, Vascotto F, Hefesha H, Grunwitz C, Vormehr M, Hüsemann Y, Selmi A, Kuhn AN, Buck J, Derhovanessian E, Rae R, Attig S, Diekmann J, Jabulowsky RA, Heesch S, Hassel J, Langguth P, Grabbe S, Huber C, Türeci Ö, Sahin U.

Lymphoid organs, in which antigen presenting cells (APCs) are in close proximity to T cells, are the ideal microenvironment for efficient priming and amplification of T-cell responses. However, the systemic delivery of vaccine antigens into dendritic cells (DCs) is hampered by various technical challenges. Here we show that DCs can be targeted precisely and effectively in vivo using intravenously administered RNA-lipoplexes (RNA-LPX) based on well-known lipid carriers by optimally adjusting net charge, without the need for functionalization of particles with molecular ligands. The LPX protects RNA from extracellular ribonucleases and mediates its efficient uptake and expression of the encoded antigen by DC populations and macrophages in various lymphoid compartments. RNA-LPX triggers interferon-α (IFNα) release by plasmacytoid DCs and macrophages. Consequently, DC maturation in situ and inflammatory immune mechanisms reminiscent of those in the early systemic phase of viral infection are activated. We show that RNA-LPX encoding viral or mutant neo-antigens or endogenous self-antigens induce strong effector and memory T-cell responses, and mediate potent IFNα-dependent rejection of progressive tumours. A phase I dose-escalation trial testing RNA-LPX that encode shared tumour antigens is ongoing. In the first three melanoma patients treated at a low-dose level, IFNα and strong antigen-specific T-cell responses were induced, supporting the identified mode of action and potency. As any polypeptide-based antigen can be encoded as RNA, RNA-LPX represent a universally applicable vaccine class for systemic DC targeting and synchronized induction of both highly potent adaptive as well as type-I-IFN-mediated innate immune mechanisms for cancer immunotherapy.

PMID: 27281205 [PubMed - indexed for MEDLINE]

Science. 2016 Jun 10;352(6291):1337-41.

Targeting of cancer neoantigens with donor-derived T cell receptor repertoires.

Strønen E, Toebes M, Kelderman S, van Buuren MM, Yang W, van Rooij N, Donia M, Böschen ML, Lund-Johansen F, Olweus J, Schumacher TN.

Accumulating evidence suggests that clinically efficacious cancer immunotherapies are driven by T cell reactivity against DNA mutation-derived neoantigens. However, among the large number of predicted neoantigens, only a minority is recognized by autologous patient T cells, and strategies to broaden neoantigen-specific T cell responses are therefore attractive. We found that naïve T cell repertoires of healthy blood donors provide a source of neoantigen-specific T cells, responding to 11 of 57 predicted human leukocyte antigen (HLA)-A*02:01-binding epitopes from three patients. Many of the T cell reactivities involved epitopes that in vivo were neglected by patient autologous tumor-infiltrating lymphocytes. Finally, T cells redirected with T cell receptors identified from donor-derived T cells efficiently recognized patient-derived melanoma cells harboring the relevant mutations, providing a rationale for the use of such "outsourced" immune responses in cancer immunotherapy.

PMID: 27198675 [PubMed - indexed for MEDLINE]

Oncology (Williston Park). 2016 May;30(5):475-81, 485.

Injecting Hope--A Review of Breast Cancer Vaccines.

Mittendorf EA, Peoples GE.

Comment in

Oncology (Williston Park). 2016 May;30(5):486-7.

There is significant interest in investigating immunotherapeutic strategies to be used for the treatment of breast cancer patients. One form of immunotherapy under active investigation is the cancer vaccine. Vaccines are a form of active immune therapy designed to stimulate the immune system to recognize tumor cells as foreign. Vaccines include an antigen that serves as the target for the immune response, and an immunoadjuvant, which is a nonspecific stimulator of the immune response that promotes an environment conducive to immune stimulation. Vaccines are an appealing therapeutic strategy because they are specific and are associated with minimal toxicity. In addition, they stimulate the adaptive immune system, thereby producing a memory response allowing for sustained effect without repeated therapy. Currently, there are no US Food and Drug Administration-approved breast cancer vaccines; however, there are multiple vaccines and treatment strategies employing these vaccines that are being actively investigated in clinical trials.

PMID: 27188680 [PubMed - indexed for MEDLINE]

Nat Med. 2016 Apr;22(4):340-1.

A liquid biopsy for cancer immunotherapy.

Schumacher TN, Scheper W.

Comment on
Nat Med. 2016 Apr;22(4):433-8.

DOI: 10.1038/nm.4074
PMID: 27050586 [PubMed - indexed for MEDLINE]

Nat Immunol. 2016 Apr;17(4):364-8.

Emerging concepts of T cell metabolism as a target of immunotherapy.

Chang CH, Pearce EL.

T cells have a pivotal protective role in defense against infection and cancer but also are instrumental in the development of many autoimmune diseases. The regulation of nutrient uptake and utilization in T cells is critically important for the control of their differentiation, and manipulating metabolic pathways in these cells can alter their function and longevity. While the importance of T cell metabolic remodeling in different physiological settings is not fully understood, there is a growing realization that inappropriate metabolic remodeling underlies many aberrant immune responses and that manipulating cellular metabolism can beneficially enhance or temper immunity. Here we comment on the basic metabolic pathways in T cells, followed by a discussion on up-to-date findings about the relationship between metabolism and T cell function and longevity. Furthermore, we expand on potential approaches and applications in which T cells might be manipulated by the reprogramming of metabolic pathways for therapeutic purposes.

PMCID: PMC4990080
PMID: 27002844 [PubMed - indexed for MEDLINE]

Cancer Treat Rev. 2016 Apr;45:68-75.

New perspectives on complement mediated immunotherapy.

Stasiłojć G, Österborg A, Blom AM, Okrój M.

Tumor-specific monoclonal antibodies (mAbs) offer several modes of tumor cell killing, from direct cytotoxic activity to indirect mechanisms employing the host immune system, particularly its innate branch. The latter effector functions seem to dominate among clinically approved anti-cancer mAbs and major efforts are being undertaken by both academia and the pharmaceutical industry with the aim to improve complement activation, antibody-dependent cellular cytotoxicity (ADCC) and Fc/opsonin-mediated phagocytosis. On one hand, there are a variety of available effector mechanisms to allow multistep elimination of tumor cells. On the other hand, tumor cells adopt a number of strategies to evade immune attack, such as overexpression of complement inhibitors, trogocytosis, shedding or internalization of mAb-targeted epitopes, which all contribute to their resistance against host defense mechanisms. Another problem recognized only recently is the depletion of immune effectors during the first round of treatment, which in concordance with delayed turnover of immune components renders subsequent rounds of therapy ineffective. Herein, we discuss newly identified limiting factors but also novel mechanistic data on complement activation by antitumor antibodies as issues important for guidance towards the next generations of immunotherapeutics.

PMID: 26994325 [PubMed - indexed for MEDLINE]

Nat Rev Drug Discov. 2016 Apr;15(4):235-47.

Development of immuno-oncology drugs - from CTLA4 to PD1 to the next generations.

Hoos A.

Since the regulatory approval of ipilimumab in 2011, the field of cancer immunotherapy has been experiencing a renaissance. This success is based on progress in both preclinical and clinical science, including the development of new methods of investigation. Immuno-oncology has become a sub-specialty within oncology owing to its unique science and its potential for substantial and long-term clinical benefit. Immunotherapy agents do not directly attack the tumour but instead mobilize the immune system - this can be achieved through various approaches that utilize adaptive or innate immunity. Therefore, immuno-oncology drug development encompasses a broad range of agents, including antibodies, peptides, proteins, small molecules, adjuvants, cytokines, oncolytic viruses, bi-specific molecules and cellular

therapies. This Perspective summarizes the recent history of cancer immunotherapy, including the factors that led to its success, provides an overview of novel drug-development considerations, summarizes three generations of immunotherapies that have been developed since 2011 and, thus, illustrates the breadth of opportunities these new generations of immunotherapies represent.

DOI: 10.1038/nrd.2015.35
PMID: 26965203 [PubMed - indexed for MEDLINE]

Arch Pathol Lab Med. 2016 Mar; 140(3):245-8.

Next-Generation Sequencing and Immunotherapy Biomarkers: A Medical Oncology Perspective.

Bernicker E.

The two most important scientific developments of the past decade regarding therapies for patients with non-small cell lung cancer are the ability to exploit particular genetic mutations with targeted therapies and the discovery of drugs that can help the patient's own immune system attack the cancer. Despite these advances, many patients do not yet benefit from either approach. To maximize patient benefit, clinicians and pathologists will need to rationally apply the growing scientific knowledge to best characterize a patient's tumor and possible driver mutations. A growing understanding of host-tumor immune interactions will hopefully help expand our therapeutic options. Lastly, the still elusive identification of immunotherapy biomarkers will hopefully help identify patients most likely to derive a therapeutic response to immune checkpoint inhibitors, and promises to be an important field of study for years to come.

PMID: 26927719 [PubMed - indexed for MEDLINE]

Acta Gastroenterol Belg. 2016 Apr-Jun;79(2):186-90.

Usefulness of IT knife nano for endoscopic submucosal dissection of large colo-rectal lesions.

Suzuki T, Hara T, Kitagawa Y, Yamaguchi T.

AIM: Endoscopic submucosal dissection (ESD) is currently widely conducted for the treatment of early gastrointestinal -cancers. Due to the characteristic anatomy of the large intestine, needle- tip type devices such as Dual knife are mainly used in colorectal ESD. On the other hand, the non- needle-tip type IT knife is a unique device with an insulated tip, and has been reported to be safe, efficacious and speedy when used in gastric ESD. A new model of IT knife, IT knife nano, anticipated to be useful for esophageal and colorectal ESD has become available, but its usefulness has not been reported. Therefore, we performed this study to evaluate the usefulness of IT knife nano for ESD of large colorectal lesions. METHOD: Previous studies have shown that a tumor size of 40 mm or above significantly prolongs treatment time and is a factor of treatment difficulty. We selected colorectal lesions of 40 mm and above, and compared 32 lesions treated with Dual knife alone before IT knife nano was available (No-IT group) and 40 cases treated with IT knife nano as a second knife after IT knife nano became available (IT group). We assessed en bloc resection rate, complete en bloc resection rate, complication rate and treatment time. RESULTS: The en bloc resection rates in No-IT group and IT group were 100% and 97.5%, respectively, with no significant difference. The respective median treatment time was 70 min and 51 min, and was significantly shortened in IT group ($P < 0.05$). The respective rates of procedure- related perforation were 3.1% and 0% ; in IT group suggesting a tendency of reduced incidence. CONCLUSIONS: Use of IT knife nano in ESD for large colorectal -lesions achieves the same levels of efficacy and safety as conventional device, with the additional merit of shortening treatment time.

PMID: 27382935 [PubMed - indexed for MEDLINE]

Ann Thorac Surg. 2016 Mar;101(3):1230-7.

The Society of Thoracic Surgeons Expert Consensus Statement: A Tool Kit to Assist Thoracic Surgeons Seeking Privileging to Use New Technology and Perform Advanced Procedures in General Thoracic Surgery.

Blackmon SH, Cooke DT, Whyte R, Miller D, Cerfolio R, Farjah F, Rocco G, Blum M, Hazelrigg S, Howington J, Low D, Swanson S, Fann JI, Ikonomidis JS, Wright C, Grondin SC.

PMID: 27124326 [PubMed - indexed for MEDLINE]

Am J Surg. 2016 Apr;211(4):778-82.

Laparoscopic antrectomy: a safe and definitive treatment in managing type 1gastric carcinoids.

Jenny HE, Ogando PA, Fujitani K, Warner RR, Divino CM.

BACKGROUND: Treatment for type 1 gastric carcinoid (T1GC) includes esophagogastroduodenoscopy (EGD), polypectomy, and antrectomy, but few studies compare outcomes. This study assessed risk-benefit ratio to determine the most effective treatment for T1GC. METHODS: A retrospective review of 52 T1GC patients (ages 30 to 88 years; 77% female) presenting to Mount Sinai Medical Center between 2004 and 2012 was conducted. Patient demographics, procedures, and outcomes were reviewed, and patient satisfaction was assessed using a phone-administered validated questionnaire. Data were analyzed using SPSS version 20 software. RESULTS: Average EGDs needed per follow-up year was significantly lower for antrectomy than polypectomy or EGD surveillance (.395 vs 1.038 vs 1.380, P = .002). Antrectomy patients exhibited decreased recurrence risk than polypectomy patients (11% vs 44%, P = .049), despite longer follow-up time (6.10 vs 4.39 years, P = .023). CONCLUSIONS: Antrectomy treats T1GC with lower recurrence risk and less postintervention monitoring, whereas allowing patients to avoid the discomfort of repeated EGD surveillance and anxiety over a lingering condition.

PMID: 26992358 [PubMed - indexed for MEDLINE]

Eur J Surg Oncol. 2016 May;42(5):604-15.

Patterns and outcomes of breast reconstruction in older women - A systematic review of the literature.

Oh DD, Flitcroft K, Brennan ME, Spillane AJ.

PURPOSE: Older age is associated with lower rates of breast reconstruction (BR) for women requiring mastectomy. The purpose was to assess the available evidence on uptake, outcome and quality of life (QoL) after BR in older women. METHODS: A systematic literature review was performed via Medline, Embase and Cochrane databases using the search terms breast reconstruction, breast cancer, and mastectomy. Eligible studies reported rates of BR, rates of different reconstructive techniques, complication rates, and/or patient reported outcome measures (PROMs) of BR in women aged 60 years or older undergoing mastectomy for ductal carcinoma in situ or invasive carcinoma. RESULTS: A total of 42 eligible studies were included, with 32 of these reporting BR rates, 10 reporting rates of different reconstructive techniques, 10 reporting rates of complications, and four reporting PROMs. The studies reported 24,746 cases of BR in 407,570 mastectomy patients aged 60 years or older from 1987 to 2012. Implant based BR was more common than autologous techniques. Mostly, complication rates were not higher in older women, and QoL outcomes were similar to younger women. CONCLUSIONS: This review confirms that BR rates are lower in older women despite recent studies demonstrating its efficacy. The perception among some surgeons and women requiring mastectomy that the potential risks of BR in older women outweigh the benefits needs to be revisited. Education of consumers and surgeons along with public advocacy for offering BR to all clinically eligible women are the most promising means of changing practice.

PMID: 26965305 [PubMed - indexed for MEDLINE]

Eur J Surg Oncol. 2016 May;42(5):625-30.

Oncoplastic breast conserving surgery and oncological outcome: Systematic review.

Yiannakopoulou EC, Mathelin C.

Oncoplastic surgery consists a new approach for extending breast conserving surgery possibilities This manuscript aimed to systematically review data on the oncological outcome of oncoplastic breast surgery. Electronic databases were searched with the appropriate search term up to and included April 2013.INCLUSION CRITERIA: full publications including at least 10 patients and providing evidence on at least one of the following outcomes: margin involvement, local recurrence, metastatic disease, death number. Forty studies including 2830 patients, met

inclusion criteria; twenty one studies investigated volume displacement techniques; fifteen studies investigated volume replacement techniques; four studies presented data on various oncoplastic techniques. Study quality was low. The majority of studies were observational studies. The length of follow up was relatively short, with only two studies reporting a median duration longer than 60 months. Only seven studies including more than 100 patients. There was great variation in the frequency of margin involvement ranging between 0% and 36% of patients. Local recurrence was observed in 0-10.8% of patients. Distant metastasis was observed in 0-18.9% of patients. In conclusion, long term oncological outcome of oncoplastic surgery for breast cancer is not adequately investigated. Further research efforts should focus on Level I evidence on oncological outcome of oncoplastic surgery.

PMID: 26922045 [PubMed - indexed for MEDLINE]

Hepatogastroenterology. 2015 Jun;62(140):1037-40.

A Novel "Artery First" Approach Allowing Safe Resection in Laparoscopic Pancreaticoduodenectomy: The Uncinate Process First Approach.

Nagakawa Y, Hosokawa Y, Sahara Y, Takishita C, Nakajima T, Hijikata Y, Tago T, Kasuya K, Tsuchida A.

BACKGROUND/AIMS: Laparoscopic pancreaticoduodenectomy (LPD) is still a challenging operation, particularly because the dissection around the superior mesenteric artery (SMA) and bleeding control are difficult. Although it has been reported that early ligation of the origin of the inferior pancreaticoduodenal artery (IPDA) reduces blood loss, it is difficult to laparoscopically expose the origin of the IPDA. We sought to develop a novel approach to simplify the dissection of the IPDA and reduce bleeding. METHODOLOGY: The uncinate process was exposed at the left posterior side of the SMA, and the branches of the IPDA were divided at positions where they enter and exit the uncinate process before isolating the pancreatic head from the right aspect of the SMA. Ten patients were operated using this new approach, and the results were retrospectively compared to those of 22 patients treated with conventional LPD. RESULTS: The operation times did not differ significantly between the two groups. However, the intraoperative blood loss was significantly lower in the "uncinated process first" group than in the conventional LPD group. (162.7 ml vs. 463.8 ml, respectively; P = 0.023). CONCLUSIONS: The new approach facilitates the initial dissection of the IPDA at the right side of the SMA, reducing intraopera- tive blood loss.

PMID: 26902052 [PubMed - indexed for MEDLINE]

Ann Surg Oncol. 2016 May;23(5):1418-9

A New Technology for Sentinel Node Biopsy: A Logistic Improvement.

Blair SL.

Comment on
Ann Surg Oncol. 2016 May;23(5):1508-14.

PMID: 26893223 [PubMed - indexed for MEDLINE]

J Clin Oncol. 2016 Apr 1;34(10):1087-96.

Comparative Effectiveness of Minimally Invasive Hysterectomy for Endometrial Cancer.

Wright JD, Burke WM, Tergas AI, Hou JY, Huang Y, Hu JC, Hillyer GC, Ananth CV, Neugut AI, Hershman DL.

PURPOSE: Despite the potential benefits of minimally invasive hysterectomy for uterine cancer, population-level data describing the procedure's safety in unselected patients are lacking. We examined the use of minimally invasive surgery and the association between the route of the procedure and long-term survival. METHODS: We used the SEER-Medicare database to identify women with stage I-III uterine cancer who underwent hysterectomy from 2006 to 2011. Patients who underwent abdominal hysterectomy were compared with those who had minimally invasive hysterectomy (laparoscopic and robot-assisted). Perioperative morbidity, use of adjuvant therapy, and long-term survival were examined after propensity score balancing. RESULTS: We identified 6,304 patients, including 4,139 (65.7%) who underwent abdominal hysterectomy and 2,165 (34.3%) who underwent minimally invasive hysterectomy; performance of minimally invasive hysterectomy increased from 9.3% in 2006 to 61.7% in 2011. Robot-assisted procedures accounted for 62.3% of the minimally invasive operations. Compared with women who underwent abdominal hysterectomy, minimally invasive hysterectomy was associated with a lower overall complication rate (22.7% v 39.7%; P < .001), and lower perioperative mortality (0.6% v 1.1%), but these women were more likely to receive adjuvant pelvic radiotherapy (34.3% v 31.3%) and brachytherapy (33.6% v 31.0%; P < .05). The complication rate was higher after robot-assisted hysterectomy compared with laparoscopic hysterectomy (23.7% v 19.5%; P = .03). There was no association between the use of minimally

invasive hysterectomy and either overall (HR, 0.89; 95% CI, 0.75 to 1.04) or cancer-specific (HR, 0.83; 95% CI, 0.59 to 1.16) mortality. CONCLUSION: Minimally invasive hysterectomy does not appear to compromise long-term survival for women with endometrial cancer.

PMCID: PMC4872018 [Available on 2017-02-01]
PMID: 26834057 [PubMed - indexed for MEDLINE]

J Thorac Cardiovasc Surg. 2016 Feb;151(2):e33-4.

Something old, something new: Marrying 2 approaches to resect an ectopic parathyroid adenoma.

Dinga Madou I, Callender GG, Kim AW.

Comment in
J Thorac Cardiovasc Surg. 2016 Feb;151(2):e35-6.

PMID: 26806514 [PubMed - indexed for MEDLINE]

Medicine (Baltimore). 2016 Jan;95(2):e2456.

A New Surgical Procedure "Dumbbell-Form Resection" for Selected Hilar Cholangiocarcinomas With Severe Jaundice: Comparison With Hemihepatectomy.

Wang S, Tian F, Zhao X, Li D, He Y, Li Z, Chen J.

The aim of the study is to evaluate the therapeutic effect of a new surgical procedure, dumbbell-form resection (DFR), for hilar cholangiocarcinoma (HCCA) with severe jaundice. In DFR, liver segments I, IVb, and partial V above the right hepatic pedicle are resected.Hemihepatectomy is recognized as the preferred procedure; however, its application is limited in HCCAs with severe jaundice.Thirty-eight HCCA patients with severe jaundice receiving DFR and 70 receiving hemihepatectomy from January 2008 to January 2013 were included. Perioperative parameters, operation-related morbidity and mortality, and post-operative survival were analyzed.A total of 21.1% patients (8/38) in the DFR group received percutaneous transhepatic biliary drainage (PTBD), which was significantly <81.4% (57/70) in the hemihepatectomy group. The TBIL was higher in the DFR group at operation (243.7 vs 125.6μmol/L, respectively). The remnant liver volume was significantly higher after DFR. The operation-related morbidity was significantly

lower after DFR than after hemihepatectomy (26.3% vs 48.6%, respectively). None of the patients died during the perioperative period after DFR, whereas 3 died after hemihepatectomy. There was no difference in margin status, histological grade, lymph-node involvement, and distant metastasis between the 2 groups. The 1-, 3-, and 5-year survival rates after DFR (68.4%, 32.1%, and 21.4%, respectively) showed no significant difference with those after hemihepatectomy (62.7%, 34.6%, and 23.3%, respectively). Kaplan-Meier analysis indicated that overall survival and recurrence after DFR demonstrated no significant difference compared with hemihepatectomy.DFR appears to be feasible for selected HCCA patients with severe jaundice. However, its indications should be restricted.

PMCID: PMC4718265
PMID: 26765439 [PubMed - indexed for MEDLINE]

J Craniofac Surg. 2016 Jan;27(1):e82-5.

A Comparison of Free Tissue Transfers to the Head and Neck Performed by Sugeons and Otolaryngologists.

Kordahi AM, Hoppe IC, Lee ES.

BACKGROUND: The reconstruction of defects resulting from the extirpation of head and neck neoplasms is performed by both otolaryngology and plastic surgery services, mostly dependent on the institution. The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) provides a unique opportunity to examine a predefined set of variables with regard to free vascularized tissue transfers performed by each service. METHODS: Following institutional review board approval, the NSQIP Participant Use Files for 2005 to 2011 were examined for all Current Procedural Terminology codes regarding free tissue transfer and with primary ICD-9 codes indicating a head and neck neoplasm. Each record was examined to determine which service performed the free tissue reconstruction and subsequent outcomes. RESULTS: During this time period a total of 534 flaps were performed, 213 by plastic surgery and 321 by otolaryngology. Total hospital length of stay was 12.9 and 11.2 days for plastic surgery and otolaryngology, respectively ($P < 0.05$). There were no significant differences noted between surgical site infections, wound dehiscence, and flap failure. Patients undergoing flaps performed by plastic surgery were significantly more likely to be on a ventilator 48 hours postoperatively ($P < 0.005$). Plastic surgery performed a significantly increased number of osseous flaps compared with otolaryngology ($P < 0.05$). CONCLUSIONS: This study shows similar results with regard to free vascularized tissue transfers when performed by plastic surgery and otolaryngology. Slightly longer hospital stays and longer time spent on the

ventilator may be associated with the increased number of osseous flaps performed by plastic surgery.

PMID: 26703037 [PubMed - indexed for MEDLINE]

Dermatol Surg. 2016 Jan;42(1):109-14.

Versatility of the O-Z Flap in the Reconstruction of Facial Defects.

Regula CG, Liu A, Lawrence N.

BACKGROUND: The O-Z flap has traditionally been used for surgical defects adjacent to critical anatomic structures requiring a repair option that minimizes distortion and functional impairment. However, another advantage of the O-Z flap is that it is tissue conservative, particularly in comparison to primary closure. In fact, the design simply takes the Burow's triangles that would be discarded and rotates them inward. OBJECTIVE: The purpose of this work is to detail the type of post-Mohs defects, which might benefit from consideration of the O-Z flap with emphasis on tissue conservation and restoration of contour to the surgical site. Furthermore, the authors wish to describe unique considerations in each location and methods to appropriately plan the O-Z flap in each circumstance. METHODS AND MATERIALS: The authors reviewed all flaps classified as O-Z in their tumor registry. The approximate size of the defect reconstructed, complications, and long-term outcomes were recorded. RESULTS: O-Z flap implementation is described in detail for repair of defects located at the lateral nasal tip, nose-cheek junction, medial canthus, and mid-cheek. CONCLUSION: The O-Z flap can be effectively used to repair defects located at the lateral nasal tip, nose-cheek junction, medial canthus, and mid-cheek. It is a mechanically simple flap with predictable tension vectors, which can be specifically oriented to protect the free margin.

PMID: 26673431 [PubMed - indexed for MEDLINE]

Medicine (Baltimore). 2015 Dec;94(49):e1922.

Robotic Total Gastrectomy With Intracorporeal Robot-Sewn Anastomosis: A Novel Approach Adopting the Double-Loop Reconstruction Method.

Parisi A, Ricci F, Trastulli S, Cirocchi R, Gemini A, Grassi V, Corsi A, Renzi C, De Santis F, Petrina A, Pironi D, D'Andrea V, Santoro A, Desiderio J.

Gastric cancer constitutes a major health problem. Robotic surgery has been progressively developed in this field. Although the feasibility of robotic procedures has been demonstrated, there are unresolved aspects being debated, including the reproducibility of intracorporeal in place of extracorporeal anastomosis. Difficulties of traditional laparoscopy have been described and there are well-known advantages of robotic systems, but few articles in literature describe a full robotic execution of the reconstructive phase while others do not give a thorough explanation how this phase was run. A new reconstructive approach, not yet described in literature, was recently adopted at our Center. Robotic total gastrectomy with D2 lymphadenectomy and a so-called "double-loop" reconstruction method with intracorporeal robot-sewn anastomosis (Parisi's technique) was performed in all reported cases. Preoperative, intraoperative, and postoperative data were collected and a technical note was documented. All tumors were located at the upper third of the stomach, and no conversions or intraoperative complications occurred. Histopathological analysis showed R0 resection obtained in all specimens. Hospital stay was regular in all patients and discharge was recommended starting from the 4th postoperative day. No major postoperative complications or reoperations occurred. Reconstruction of the digestive tract after total gastrectomy is one of the main areas of surgical research in the treatment of gastric cancer and in the field of minimally invasive surgery. The double-loop method is a valid simplification of the traditional technique of construction of the Roux-limb that could increase the feasibility and safety in performing a full hand-sewn intracorporeal reconstruction and it appears to fit the characteristics of the robotic system thus obtaining excellent postoperative clinical outcomes.

PMID: 26656323 [PubMed - indexed for MEDLINE]

Thorac Surg Clin. 2016 Feb;26(1):13-8.

Open Surgical Approaches for Pulmonary Metastasectomy.

Downey RJ , Bains MS.

Surgeons differ in the approach to resection of pulmonary metastases from nonpulmonary primary malignancies, with some favoring procedures that minimize trauma to the patient, and others performing open procedures with the goal of maximizing likelihood of resection of all detectable sites of disease. This article reviews how pulmonary metastasectomy emerged as a therapy for metastatic disease. Discussed is how surgical approaches used for this procedure have evolved, the available literature addressing whether open procedures lead to more complete resections, and if so whether resection by open procedures increases the likelihood of

cure following resection. The technical aspects of the various thoracotomy techniques are also reviewed.

PMID: 26611506 [PubMed - indexed for MEDLINE]

Cancer Treat Res. 2016;167:149-79.

Surgical Management of Melanoma.

Koshenkov VP, Broucek J, Kaufman HL.

The surgical management of melanoma has undergone considerable changes over the past several decades, as new strategies and treatments have become available. Surgeons play a pivotal role in all aspects of melanoma care: diagnostic, curative, and palliative. There is a high potential for cure in patients with early-stage melanoma and the selection of an appropriate operation is very important for this reason. Staging the nodal basin has become widespread since the adoption of sentinel lymph node biopsy (SLNB) for the management of melanoma. This operation provides the best prognostic information that is currently available for patients with melanoma. The surgeon plays a central role in the palliation of symptoms resulting from nodal disease and metastases, as melanoma has a propensity to spread to almost any site in the body.

PMID: 26601862 [PubMed - indexed for MEDLINE]

J Plast Reconstr Aesthet Surg. 2016 Feb;69(2):206-10.

Immediate two-stage nipple reconstruction with a local mastectomy flap following secondary autologous breast reconstruction.

He J, Wang T, Xu H, Zhang Y, Dong J.

Because of the inevitable postoperative shrinkage, an initial hypercorrection is emphasized in nipple reconstruction with a random skin flap. However, the breast shape will be damaged if an excessively large flap is raised on the surface of the breast mound. A technique for immediate two-stage nipple reconstruction with a local mastectomy flap during the secondary breast reconstruction was reported in this study. From February 2011 to March 2014, 33 patients

underwent breast reconstruction and immediate two-stage nipple reconstructions. A bipedicle deep inferior epigastric artery perforator (DIEP) flap was raised and folded upward to form the breast. Simultaneously, a deepithelialized lower mastectomy flap with a distant skin paddle was elevated and pulled throughout the reconstructed breast. The skin paddle was carefully sutured to the position of the future nipple. After 3 weeks, the pedicle of the mastectomy flap was divided, and the paddle was modeled to form the new nipple. Both the new nipple and the DIEP flaps survived postoperatively. The average projection of the reconstructed nipple was 15.4 ± 2.7 mm immediately after the surgery, which gradually decreased to 8.2 ± 1.1 mm during the first year of follow-up. A total of 29 patients ranked the aesthetic appearance of the reconstructed nipple and breast as "very good" or "good." On the basis of our breast-shaping techniques, the proposed immediate two-stage nipple reconstruction approach is able to maintain long-term residual projection and results in considerable patient satisfaction. LEVEL OF EVIDENCE: IV.

PMID: 26584838 [PubMed - indexed for MEDLINE]

Ann Surg. 2015 Nov;262(5):831-9; discussion 829-40.

Laparoscopic Versus Open Surgery for Gastric Gastrointestinal Stromal Tumors: What Is the Impact on Postoperative Outcome and Oncologic Results?

Piessen G, Lefèvre JH, Cabau M, Duhamel A, Behal H, Perniceni T, Mabrut JY, Regimbeau JM, Bonvalot S, Tiberio GA, Mathonnet M, Regenet N, Guillaud A, Glehen O, Mariani P, Denost Q, Maggiori L, Benhaim L, Manceau G, Mutter D, Bail JP, Meunier B, Porcheron J, Mariette C, Brigand C; AFC and the FREGAT working group.

OBJECTIVES: The aim of the study was to compare the postoperative and oncologic outcomes of laparoscopic versus open surgery for gastric gastrointestinal stromal tumors (gGISTs). BACKGROUND: The feasibility of the laparoscopic approach for gGIST resection has been demonstrated; however, its impact on outcomes, particularly its oncologic safety for tumors greater than 5cm, remains unknown. METHODS: Among 1413 patients treated for a GIST in 61 European centers between 2001 and 2013, patients who underwent primary resection for a gGIST smaller than 20cm (N=666), by either laparoscopy (group L, n=282) or open surgery (group O, n=384), were compared. Multivariable analyses and propensity score matching were used to compensate for differences in baseline characteristics. RESULTS: In-hospital mortality and morbidity rates in groups L and O were 0.4% versus 2.1% (P=0.086) and 11.3% vs 19.5% (P=0.004), respectively. Laparoscopic resection was independently protective against in-hospital morbidity (odds ratio 0.54, P=0.014). The rate of R0 resection was 95.7% in group L

and 92.7% in group O (P=0.103). After 1:1 propensity score matching (n=224), the groups were comparable according to age, sex, tumor location and size, mitotic index, American Society of Anesthesiology score, and the extent of surgical resection. After adjustment for BMI, overall morbidity (10.3% vs 19.6%; P=0.005), surgical morbidity (4.9% vs 9.8%; P=0.048), and medical morbidity (6.2% vs 13.4%; P=0.01) were significantly lower in group L. Five-year recurrence-free survival was significantly better in group L (91.7% vs 85.2%; P=0.011). In tumors greater than 5cm, in-hospital morbidity and 5-year recurrence-free survival were similar between the groups (P=0.255 and P=0.423, respectively). CONCLUSIONS: Laparoscopic resection for gGISTs is associated with favorable short-term outcomes without compromising oncologic results.

PMID: 26583673 [PubMed - indexed for MEDLINE]

Am J Obstet Gynecol. 2016 Apr;214(4):503.e1-6.

Minimally invasive interval debulking surgery in ovarian neoplasm (MISSION trial-NCT02324595): a feasibility study.

Gueli Alletti S , Bottoni C, Fanfani F, Gallotta V, Chiantera V, Costantini B, Cosentino F, Ercoli A, Scambia G, Fagotti A.

BACKGROUND: Laparoscopy has acquired an increasing role in the management of ovarian cancer. Laparoscopic cytoreduction could represent a new frontier for selected patients after neoadjuvant chemotherapy (NACT). OBJECTIVE: We sought to assess feasibility and early complication rate of minimally invasive (MI) interval debulking surgery (IDS) in stage III-IV epithelial ovarian cancer (EOC) patients after NACT. STUDY DESIGN: This is a phase II multicentric study in advanced EOC cases with clinical complete response after NACT, according to Gynecologic Cancer Intergroup and Response Evaluation Criteria In Solid Tumors criteria. Institutional review board approval was obtained and all patients signed written informed consent to be included in the protocol. The study was registered in clinicaltrials.gov (NCT02324595) and was named "MISSION" trial. For patients meeting inclusion criteria, surgical procedures started with diagnostic laparoscopy to confirm preoperative findings and assess surgical complexity. MI-IDS included hysterectomy, bilateral salpingo-oophorectomy, appendectomy, omentectomy, peritonectomy, and bowel resection. Pelvic and/or aortic lymphadenectomy was not considered as standard procedure in these cases. Intraoperative and postoperative outcomes, time to restart chemotherapy, survival rate, and quality of life data were registered. RESULTS: From December 2013 through February 2015, of 184 advanced EOC patients considered eligible for IDS, 52 (28.2%) met inclusion criteria and were enrolled in

the study. For 22 (12%) of them, standard laparotomic approach was preferred because of intraoperative surgeon evaluation. Thirty (16.3%) patients received the planned treatment of MI-IDS. Median age was 61 (range 39-81) years and median body mass index was 24 (range 20-31) kg/m(2). Median numbers of NACT cycles was 4 (range 3-7). Median operative time was 285 (range 124-418) minutes and median estimated blood loss was 100 (range 50-200) mL. Surgical procedures included 28 (93.3%) hysterectomy and bilateral salpingo-oophorectomy, 29 (96.6%) omentectomy, 2 (6.6%) appendectomy, 11 (36.6%) regional peritonectomy, and 1 (3.4%) bowel resection. A residual tumor of 0 cm was reached in 29 (96.6%) patients and 0.5 cm in only 1 (3.4%) case. The vast majority of patients were discharged on postoperative day 2 (range 2-3). No early postoperative complications were registered. Median time to restart chemotherapy was 20 (10-30) days and all patients successfully completed the cycles. Histological findings showed 3 (10%) complete response, 9 (30%) microscopic residual disease, and 18 (60%) evidence of macroscopic residual disease. With a median follow-up of 10.5 month, 5 peritoneal and 2 lymph nodal recurrences were observed. Psychometric test revealed moderate discomfort in the vast majority of patients (66.7%). All patients are still alive. CONCLUSION: Invasive-IDS in patients with clinically complete response to NACT seems to be feasible and safe in terms of perioperative outcomes, psycho-oncological impact, and survival rate. The equivalence between MI surgery and laparotomy needs to be confirmed with a longer follow-up and a larger number of patients.

PMID: 26529370 [PubMed - indexed for MEDLINE]

JAMA Oncol. 2016 Jan;2(1):112-7.

Comparison of Adverse Events for Endoscopic vs Percutaneous Biliary Drainage in the Treatment of Malignant Biliary Tract Obstruction in an Inpatient National Cohort.

Inamdar S, Slattery E, Bhalla R, Sejpal DV, Trindade AJ.

IMPORTANCE: Nonsurgical biliary drainage in malignant biliary tract obstruction can be performed endoscopically by endoscopic retrograde cholangiopancreatography (ERCP) or by percutaneous transhepatic biliary drainage (PTBD). The published body of literature to support either approach is surprisingly sparse, is conflicting on the preferred approach, and is limited by small studies with heterogeneous groups. OBJECTIVE: To evaluate the procedure-related adverse event rate with endoscopic vs percutaneous drainage in patients with malignant biliary tract obstruction. DESIGN, SETTING, AND PARTICIPANTS: This was a retrospective analysis from the National Inpatient Sample (NIS) database from 2007 through 2009. Data analysis was performed in 2015. Patients from the NIS database are representative of the US population and

are included from both community and tertiary care hospitals in the United States. MAIN OUTCOMES AND MEASURES: Procedure-related adverse event rates. RESULTS: A total of 7445 patients were included for ERCP and 1690 for PTBD. The overall adverse event rate was 8.6% for endoscopic drainage (640 events) and 12.3% for percutaneous biliary drainage (208 events) (P < .001). When analyzed by type of malignant neoplasm, ERCP was associated with a lower rate of adverse events compared with PTBD for pancreatic cancer (2.9% vs 6.2%; odds ratio [OR], 0.46 [95% CI, 0.35-0.61]; P < .001) and cholangiocarcinoma (2.6% vs 4.2% OR, 0.62 [95% CI, 0.35-1.10]; P = .10). For pancreatic cancer, endoscopic procedures were associated with a lower rate of adverse events regardless of the volume of percutaneous procedures performed by a center. For cholangiocarcinoma, centers that performed a low volume of percutaneous biliary drainage procedures were more likely to have adverse events compared with endoscopic procedures performed at the same center (5.7% vs 2.5%; OR, 2.28 [95% CI, 1.02-5.11]; P = .04). In centers that performed a high volume of percutaneous drainage procedures, rates of adverse events were similar to those of endoscopic adverse events (3.5% vs 3.0%; OR, 1.18 [95% CI, 0.53-2.66]; P = .68). CONCLUSIONS AND RELEVANCE: Our results support the finding that endoscopic biliary drainage for malignant biliary obstruction is a first-line intervention. Endoscopic drainage is superior to percutaneous drainage, in regard to adverse event rate, for patients with pancreatic cancer. For patients with cholangiocarcinoma, endoscopic drainage is superior in centers that perform a low volume of percutaneous biliary drainage procedures.

PMID: 26513013 [PubMed - indexed for MEDLINE]

Ann Surg. 2015 Dec;262 (6):965-71.

New 3-Tiered Circumferential Resection Margin Criteria in Esophageal Squamous Cell Carcinoma.

Lee GD, Lee SE, Kim KM, Kim YH, Ahn JH, Jung S, Choi YL, Kim HR, Park SI, Shim YM.

OBJECTIVE: We aimed to investigate the optimal cutoff value of circumferential resection margin (CRM) of esophageal squamous cell carcinoma (ESCC) in patients who underwent radical esophagectomy. BACKGROUND: Tumor involvement of a CRM in ESCC has not been clearly defined. METHODS: We reviewed 479 pT3 ESCC patients to find the optimal cutoff point of distance from CRM in addition to 0μm for discriminating survival time. RESULTS: The partitions at and near the 500μm distance from CRM generated the largest log-rank statistics (P=0.0086). Therefore, we added 500μm as an additional cutoff value for a positive CRM. Compared to patients with CRM greater than 500μm, patients with CRM 0μm showed worse

overall survival (P<0.001) and progression-free survival (P<0.001), followed by patients with 0 to 500μm (P=0.008 and 0.066, respectively). In multivariable analyses, overall survival differences remained significant [0<CRM ≤ 500μm vs CRM > 500μm, hazards ratio (HR)=1.875, 97.5% CI: 1.243-2.829, P=0.002; CRM=0μm vs CRM > 500μm, HR=2.666, 97.5% CI: 1.745-4.076, P<0.001]. In comparison of criteria from the College of American Pathologists, the Royal College of Pathologists, and this study, HRs of positive CRM (95% CI, P-value) were 1.969 (1.501-2.584, P<0.001), 1.384 (1.039-1.844, P=0.027), and 1.696 (1.342-2.143, P<0.001), respectively. CONCLUSIONS: In patients with ESCC, we developed new, 3-tiered CRM criteria providing more detailed prognostic information than the 2-tiered criteria.

PMID: 26501489 [PubMed - indexed for MEDLINE]

J Surg Oncol. 2015 Dec;112(8):888-93. doi: 10.1002/jso.24073. Epub 2015 Oct 21.

Robotic gastrectomy and esophagogastrectomy: A single center experience of 105 cases.

Harrison LE, Yiengpruksawan A, Patel J, Itskovich A, Lee B, Korst R.

BACKGROUND: A robotic approach to general surgery procedures may provide improved postoperative outcomes compared to either open or laparoscopic approaches. The role of robotics for gastroesophageal surgery, however, is still being evaluated. STUDY DESIGN: A review of the prospective database for robotic surgery at Valley Hospital between January 2002 and March 2014 identified 105 patients who underwent robotic gastric and esophageal resection. Patient demographics and perioperative factors were studied. RESULTS: Over a 12 years period, 105 patients underwent robotic gastroesophageal resection. The median operative time for distal gastrectomy (230 min [112-327]) was significantly less compared to either total gastrectomy (302 min [214-364]) or esophagogastrectomy (309 min [190-682]). The length of stay for patients undergoing distal gastrectomy (6 days [4-32]) was also significantly less than patients undergoing total gastrectomy (11 days [7-43]), as well as esophagogastrectomy (9 days [5-64]). In regard to the learning curve to perform robotic gastroesophageal surgery, there was a significant correlation between operative time and overall experience. CONCLUSIONS: This study demonstrated that robotic gastroesophageal surgery is feasible and can be safely performed. Assuming familiarity with the open procedures and acquisition of basic robotic skills, the learning curve for robotic gastroesophageal surgery requires approximately 20 cases.

PMID: 26487124 [PubMed - indexed for MEDLINE]

BMJ Open. 2015 Oct 19;5(10):e008198.

Robotic, laparoscopic and open surgery for gastric cancer compared on surgical, clinical and oncological outcomes: a multi-institutional chart review. A study protocol of the International study group on Minimally Invasive surgery for GASTRIc Cancer-IMIGASTRIC.

Desiderio J, Jiang ZW, Nguyen NT, Zhang S, Reim D, Alimoglu O, Azagra JS, Yu PW, Coburn NG, Qi F, Jackson PG, Zang L, Brower ST, Kurokawa Y, Facy O, Tsujimoto H, Coratti A, Annecchiarico M, Bazzocchi F, Avanzolini A, Gagniere J, Pezet D, Cianchi F, Badii B, Novotny A, Eren T, Leblebici M, Goergen M, Zhang B, Zhao YL, Liu T, Al-Refaie W, Ma J, Takiguchi S, Lequeu JB, Trastulli S, Parisi A.

INTRODUCTION: Gastric cancer represents a great challenge for healthcare providers and requires a multidisciplinary treatment approach in which surgery plays a major role. Minimally invasive surgery has been progressively developed, first with the advent of laparoscopy and recently with the spread of robotic surgery, but a number of issues are currently being debated, including the limitations in performing an effective extended lymph node dissection, the real advantages of robotic systems, the role of laparoscopy for Advanced Gastric Cancer, the reproducibility of a total intracorporeal technique and the oncological results achievable during long-term follow-up. METHODS AND ANALYSIS: A multi-institutional international database will be established to evaluate the role of robotic, laparoscopic and open approaches in gastric cancer, comprising of information regarding surgical, clinical and oncological features. A chart review will be conducted to enter data of participants with gastric cancer, previously treated at the participating institutions. The database is the first of its kind, through an international electronic submission system and a HIPPA protected real time data repository from high volume gastric cancer centres. ETHICS AND DISSEMINATION: This study is conducted in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and relevant laws/regulations. A multicentre study with a large number of patients will permit further investigation of the safety and efficacy as well as the long-term outcomes of robotic, laparoscopic and open approaches for the management of gastric cancer. TRIAL REGISTRATION NUMBER: NCT02325453; Pre-results.

PMCID: PMC4611863
PMID: 26482769 [PubMed - indexed for MEDLINE]

J Surg Oncol. 2015 Dec;112(7):707-16.

The new era of robotic neck surgery: The universal application of the retroauricular approach.

Byeon HK, Koh YW.

Recent advances in technology has triggered the introduction of surgical robotics in the field of head and neck surgery and changed the landscape indefinitely. The advent of transoral robotic surgery and robotic thyroidectomy techniques has urged the extended applications of the robot to other neck surgeries including remote access surgeries. Based on earlier reports and our surgical experiences, this review will discuss in detail various robotic head and neck surgeries via retroauricular approach.

PMID: 26410781 [PubMed - indexed for MEDLINE]

Chest. 2016 Mar;149 (3):816-35.

Technical Aspects of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration: CHEST Guideline and Expert Panel Report.

Wahidi MM, Herth F, Yasufuku K, Shepherd RW, Yarmus L, Chawla M, Lamb C, Casey KR, Patel S, Silvestri GA, Feller-Kopman DJ.

BACKGROUND: Endobronchial ultrasound (EBUS) was introduced in the last decade, enabling real-time guidance of transbronchial needle aspiration (TBNA) of mediastinal and hilar structures and parabronchial lung masses. The many publications produced about EBUS-TBNA have led to a better understanding of the performance characteristics of this procedure. The goal of this document was to examine the current literature on the technical aspects of EBUS-TBNA as they relate to patient, technology, and proceduralist factors to provide evidence-based and expert guidance to clinicians. METHODS: Rigorous methodology has been applied to provide a trustworthy evidence-based guideline and expert panel report. A group of approved panelists developed key clinical questions by using the PICO (population, intervention, comparator, and outcome) format that addressed specific topics on the technical aspects of EBUS-TBNA. MEDLINE (via PubMed) and the Cochrane Library were systematically searched for relevant literature, which was supplemented by manual searches. References were screened for inclusion, and well-recognized document evaluation tools were used to assess the quality of included studies, to extract meaningful data, and to grade the level of evidence to support each recommendation or suggestion. RESULTS: Our systematic review and critical analysis of the literature on 15 PICO questions related to the technical aspects of EBUS-TBNA resulted in 12 statements: 7 evidence-based graded recommendations and 5 ungraded

consensus-based statements. Three questions did not have sufficient evidence to generate a statement. CONCLUSIONS: Evidence on the technical aspects of EBUS-TBNA varies in strength but is satisfactory in certain areas to guide clinicians on the best conditions to perform EBUS-guided tissue sampling. Additional research is needed to enhance our knowledge regarding the optimal performance of this effective procedure.

PMID: 26402427 [PubMed - indexed for MEDLINE]

Ann Otol Rhinol Laryngol. 2016 Mar;125(3):207-12.

Applications of Evolving Robotic Technology for Head and Neck Surgery.

Sharma A, Albergotti WG, Duvvuri U.

OBJECTIVE: Assess the use and potential benefits of a new robotic system for transoral radical tonsillectomy, transoral supraglottic laryngectomy, and retroauricular thyroidectomy in a cadaver dissection. METHODS: Three previously described robotic procedures (transoral radical tonsillectomy, transoral supraglottic laryngectomy, and retroauricular thyroidectomy) were performed in a cadaver using the da Vinci Xi Surgical System. Surgical exposure and access, operative time, and number of collisions were examined objectively. RESULTS: The new robotic system was used to perform transoral radical tonsillectomy with dissection and preservation of glossopharyngeal nerve branches, transoral supraglottic laryngectomy, and retroauricular thyroidectomy. There was excellent exposure without any difficulties in access. Robotic operative times (excluding set-up and docking times) for the 3 procedures in the cadaver were 12.7, 14.3, and 21.2 minutes (excluding retroauricular incision and subplatysmal elevation), respectively. No robotic arm collisions were noted during these 3 procedures. The retroauricular thyroidectomy was performed using 4 robotic ports, each with 8 mm instruments. CONCLUSIONS: The use of updated and evolving robotic technology improves the ease of previously described robotic head and neck procedures and may allow surgeons to perform increasingly complex surgeries.

PMID: 26391091 [PubMed - indexed for MEDLINE]

Int J Colorectal Dis. 2015 Sep;30(9):1281-3.

Use of the new Da Vinci Xi during robotic rectal resection for cancer: technical considerations and early experience.

Morelli L, Guadagni S, Di Franco G, Palmeri M, Caprili G, D'Isidoro C, Pisano R, Moglia A, Ferrari V, Di Candio G, Mosca F.

PMID: 26255257 [PubMed - indexed for MEDLINE]

Breast. 2015 Nov;24 Suppl 2:S2-5.

Progress in the surgical management of breast cancer: Present and future.

Morrow M.

Recognition of differing risks of locoregional recurrence (LRR) in breast cancer patients based on estrogen receptor, progesterone receptor, and HER2 status, coupled with a reduction in LRR in patients receiving adjuvant systemic therapy, offers the opportunity to tailor surgical treatment and reduce the morbidity of therapy. New guidelines for margins in breast-conserving therapy of tumor not touching ink and avoidance of axillary dissection in sentinel node positive patients undergoing breast-conserving therapy are examples of this approach which have entered practice. Increased use of neoadjuvant therapy offers the opportunity to identify which patients are responsive to chemotherapy prior to surgery, potentially allowing further tailoring of treatment, and ongoing clinical trials will address the question of the extent of axillary surgery and radiotherapy after neoadjuvant therapy in patients with and without pathologic complete response.

PMID: 26249120 [PubMed - indexed for MEDLINE]

Colorectal Dis. 2015 Oct;17(10):O208-12. doi: 10.1111/codi.13075.

Technique for a stapled anastomosis following transanal total mesorectal excision for rectal cancer.

Bracey E, Knol J, Buchs N, Jones O, Cunningham C, Guy R, Mortensen N, Hompes R.

AIM: Transanal total mesorectal excision (taTME) is an emerging and exciting new technique in rectal cancer surgery. As with all novel techniques, new challenges arise, requiring small modifications of the technique. Here we present a simple technique that we have devised to facilitate a stapled anastomosis using standard circular staplers following a taTME. METHOD: We describe the technique in a stepwise fashion with picture - and video illustration. Our experience with this anastomosis in a small cohort of patients is reported. RESULTS: No anastomotic leaks occurred in 12 consecutive patients using this technique following taTME. In one patient a small defect was noticed on direct visualisation of the anastomosis intra-operative, and was closed transanally. So far 8/12 patient had their protective ileostomy reversed with satisfactory function. CONCLUSION: We believe that this technique for a transanal, stapled anastomosis after a transanal TME procedure is safe and reproducible. Objective assessment of longterm functional outcome is required and outcomes need to be compared to other stapled techniques and handsewn anastomoses.

PMID: 26218610 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):549-59.

First Clinical Investigation of Cone Beam Computed Tomography and Deformable Registration for Adaptive Proton Therapy for Lung Cancer.

Veiga C, Janssens G, Teng CL, Baudier T, Hotoiu L, McClelland JR, Royle G, Lin L, Yin L, Metz J, Solberg TD, Tochner Z, Simone CB 2nd, McDonough J, Teo BK.

PURPOSE: An adaptive proton therapy workflow using cone beam computed tomography (CBCT) is proposed. It consists of an online evaluation of a fast range-corrected dose distribution based on a virtual CT (vCT) scan. This can be followed by more accurate offline dose recalculation on the vCT scan, which can trigger a rescan CT (rCT) for replanning. METHODS AND MATERIALS: The workflow was tested retrospectively for 20 consecutive lung cancer patients. A diffeomorphic Morphon algorithm was used to generate the lung vCT by deforming the average planning CT onto the CBCT scan. An additional correction step was applied to account for anatomic modifications that cannot be modeled by deformation alone. A set of clinical indicators for replanning were generated according to the water equivalent thickness (WET) and dose statistics and compared with those obtained on the rCT scan. The fast dose approximation consisted of warping the initial planned dose onto the vCT scan according to the changes in WET. The potential under- and over-ranges were assessed as a variation in WET at the target's distal surface. RESULTS: The range-corrected dose from the vCT scan reproduced clinical indicators similar to those of the rCT scan. The workflow performed well under different clinical scenarios, including atelectasis, lung reinflation, and different types of tumor response. Between the vCT and rCT scans, we found a difference in the measured 95% percentile of the over-range distribution of 3.4 ± 2.7 mm. The limitations of the technique consisted of inherent uncertainties in deformable registration and the drawbacks of CBCT imaging. The correction step was adequate when gross errors occurred but could not recover subtle anatomic or density changes in tumors with complex topology. CONCLUSIONS: A proton therapy workflow based on CBCT provided clinical indicators similar to those using rCT for patients with lung cancer with considerable anatomic changes.

PMID: 27084664 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):505-16.

Consensus Statement on Proton Therapy in Early-Stage and Locally Advanced Non-Small Cell Lung Cancer.

Chang JY, Jabbour SK, De Ruysscher D, Schild SE, Simone CB 2nd, Rengan R, Feigenberg S, Khan AJ, Choi NC, Bradley JD, Zhu XR, Lomax AJ, Hoppe BS; International Particle Therapy Co-operative Group Thoracic Subcommittee.

Radiation dose escalation has been shown to improve local control and survival in patients with non-small cell lung cancer in some studies, but randomized data have not supported this premise, possibly owing to adverse effects. Because of the physical characteristics of the Bragg peak, proton therapy (PT) delivers minimal exit dose distal to the target volume, resulting in better sparing of normal tissues in comparison to photon-based radiation therapy. This is particularly important for lung cancer given the proximity of the lung, heart, esophagus, major airways, large blood vessels, and spinal cord. However, PT is associated with more uncertainty because of the finite range of the proton beam and motion for thoracic cancers. PT is more costly than traditional photon therapy but may reduce side effects and toxicity-related hospitalization, which has its own associated cost. The cost of PT is decreasing over time because of reduced prices for the building, machine, maintenance, and overhead, as well as newer, shorter treatment programs. PT is improving rapidly as more research is performed particularly with the implementation of 4-dimensional computed tomography-based motion management and intensity modulated PT. Given these controversies, there is much debate in the oncology community about which patients with lung cancer benefit significantly from PT. The Particle Therapy Co-operative Group (PTCOG) Thoracic Subcommittee task group intends to address the issues of PT indications, advantages and limitations, cost-effectiveness, technology improvement, clinical trials, and future research directions. This consensus report can be used to guide clinical practice and indications for PT, insurance approval, and clinical or translational research directions.

PMID: 27084663 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):488-97.

Improving Outcomes for Esophageal Cancer using Proton Beam Therapy.

Chuong MD, Hallemeier CL, Jabbour SK, Yu J, Badiyan S, Merrell KW, Mishra MV, Li H, Verma V, Lin SH.

Radiation therapy (RT) plays an essential role in the management of esophageal cancer. Because the esophagus is a centrally located thoracic structure there is a need to balance the delivery of appropriately high dose to the target while minimizing dose to nearby critical structures. Radiation dose received by these critical structures, especially the heart and lungs, may lead to clinically significant toxicities, including pneumonitis, pericarditis, and myocardial infarction. Although technological advancements in photon RT delivery like intensity modulated RT have decreased the risk of such toxicities, a growing body of evidence indicates that further risk reductions are achieved with proton beam therapy (PBT). Herein we review the published dosimetric and clinical PBT literature for esophageal cancer, including motion management considerations, the potential for reirradiation, radiation dose escalation, and ongoing esophageal PBT clinical trials. We also consider the potential cost-effectiveness of PBT relative to photon RT.

PMID: 27084662 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):477-82.

Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis.

Bush DA, Smith JC, Slater JD, Volk ML, Reeves ME, Cheng J, Grove R, de Vera ME.

PURPOSE: To describe results of a planned interim analysis of a prospective, randomized clinical trial developed to compare treatment outcomes among patients with newly diagnosed hepatocellular carcinoma (HCC). METHODS AND MATERIALS: Eligible subjects had either clinical or pathologic diagnosis of HCC and met either Milan or San Francisco transplant criteria. Patients were randomly assigned to transarterial chemoembolization (TACE) or to proton beam radiation therapy. Patients randomized to TACE received at least 1 TACE with additional TACE for persistent disease. Proton beam radiation therapy was delivered to all areas of gross disease to a total dose of 70.2 Gy in 15 daily fractions over 3 weeks. The primary endpoint was progression-free survival, with secondary endpoints of overall survival, local tumor control, and treatment-related toxicities as represented by posttreatment days of hospitalization. RESULTS: At the time of this analysis 69 subjects were available for analysis. Of these, 36 were

randomized to TACE and 33 to proton. Total days of hospitalization within 30 days of TACE/proton was 166 and 24 days, respectively (P<.001). Ten TACE and 12 proton patients underwent liver transplantation after treatment. Viable tumor identified in the explanted livers after TACE/proton averaged 2.4 and 0.9 cm, respectively. Pathologic complete response after TACE/proton was 10%/25% (P=.38). The 2-year overall survival for all patients was 59%, with no difference between treatment groups. Median survival time was 30 months (95% confidence interval 20.7-39.3 months). There was a trend toward improved 2-year local tumor control (88% vs 45%, P=.06) and progression-free survival (48% vs 31%, P=.06) favoring the proton beam treatment group. CONCLUSIONS: This interim analysis indicates similar overall survival rates for proton beam radiation therapy and TACE. There is a trend toward improved local tumor control and progression-free survival with proton beam. There are significantly fewer hospitalization days after proton treatment, which may indicate reduced toxicity with proton beam therapy.

PMID: 27084661 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):435-43.

Acute Toxicity and Quality of Life in Patients With Prostate Cancer Treated With Protons or Carbon Ions in a Prospective Randomized Phase II Study--The IPI Trial.

Habl G, Uhl M, Katayama S, Kessel KA, Hatiboglu G, Hadaschik B, Edler L, Tichy D, Ellerbrock M, Haberer T, Wolf MB, Schlemmer HP, Debus J, Herfarth K.

PURPOSE: The purpose of this study was to compare safety and feasibility of proton therapy with that of carbon ion therapy in hypofractionated raster-scanned irradiation of the prostate, in a prospective randomized phase 2 trial. METHODS AND MATERIALS: In this trial, 92 patients with localized prostate cancer were enrolled. Patients were randomized to receive either proton therapy (arm A) or carbon ion therapy (arm B) and treated with a total dose of 66 Gy(relative biological effectiveness [RBE]) administered in 20 fractions (single dose of 3.3 Gy[RBE]). Patients were stratified by the use of antihormone therapy. Primary endpoint was the combined assessment of safety and feasibility. Secondary endpoints were specific toxicities, prostate-specific antigen progression-free survival (PFS), overall survival (OS), and quality of life (QoL).RESULTS: Ninety-one patients completed therapy and have had a median follow-up of 22.3 months. Among acute genitourinary toxicities, grade 1 cystitis rates were 34.1% (39.1% in A; 28.9% in B) and 17.6% grade 2 (21.7% in A; 13.3% in B). Seven patients (8%) required urinary catheterization during treatment due to urinary retention, 5 of whom were in arm A. Regarding acute gastrointestinal toxicities, 2 patients treated with protons developed grade 3

rectal fistulas. Grade 1 radiation proctitis occurred in 12.1% (13.0% in A; 11.1% in B) and grade 2 in 5.5% (8.7% in A; 2.2% in B). No statistically significant differences in toxicity profiles between arms were found. Reduced QoL was evident mainly in fatigue, pain, and urinary symptoms during therapy and 6 weeks thereafter. All European Organization for Research and Treatment of Cancer QLQ-C30 and -PR25 scores improved during follow-up. CONCLUSIONS: Hypofractionated irradiation using either carbon ions or protons results in comparable acute toxicities and QoL parameters. We found that hypofractionated particle irradiation is feasible and may be safe. Due to the occurrence of gel in the rectal wall and the consecutive occurrence of 2 rectal fistulas, we stopped using the insertion of spacer gel. Longer follow-up is necessary for evaluation of PFS and OS. (Ion Prostate Irradiation (IPI); NCT01641185; ClinicalTrials.gov.).

PMID: 27084659 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):422-34.

Five-Year Biochemical Results, Toxicity, and Patient-Reported Quality of Life After Delivery of Dose-Escalated Image Guided Proton Therapy for Prostate Cancer.

Bryant C, Smith TL, Henderson RH, Hoppe BS, Mendenhall WM, Nichols RC, Morris CG, Williams CR, Su Z, Li Z, Lee D, Mendenhall NP.

Comment in

Nat Rev Urol. 2016 Apr;13(4):181.

PURPOSE: To report clinical outcomes in patients treated with image guided proton therapy (PT) for localized prostate cancer. METHODS AND MATERIALS: The medical records of 1327 men were reviewed. Each man was enrolled on an outcomes tracking study. Dual enrollment on a prospective clinical trial was allowed. Each patient was treated for localized prostate cancer with PT at our institution between 2006 and 2010. Ninety-eight percent of patients received 78 Gy (radiobiological equivalent [RBE]) or higher; 18% received androgen deprivation therapy (ADT). The 5-year freedom from biochemical progression (FFBP), distant metastasis-free survival, and cause-specific survival rates are reported for each risk group. Data on patient-reported quality of life and high-grade toxicities were prospectively collected and reported. A multivariate analysis was performed to identify clinical predictors of biochemical failure and urologic toxicity. RESULTS: The median follow-up time was 5.5 years. The 5-year FFBP rates were 99%, 94%, and 74% in low-risk, intermediate-risk, and high-risk patients, respectively. The actuarial 5-year rates of late grade 3+ Common Terminology Criteria for Adverse Events, version 4.0, gastrointestinal (GI) and genitourinary (GU) toxicity were 0.6% and 2.9%,

respectively. Multivariate analysis showed a significant correlation between grade 3+ GU toxicity and pretreatment prostate reductive procedures (P<.0001), prostate volume (P=.0085), pretreatment α-blockers (P=.0067), diabetes (P=.0195), and dose-volume histogram parameters (P=.0208). The median International Prostate Symptom Scores pretreatment scores and scores at 5 years after treatment were 7 and 7, respectively. The mean Expanded Prostate Cancer Index Composite (EPIC) scores significantly declined for sexual summary for patients not receiving ADT (from 67 to 53) between baseline and 5 years. CONCLUSIONS: Image guided PT provided excellent biochemical control rates for patients with localized prostate cancer. The actuarial rates of high-grade toxicity were low after PT. From pretreatment to 5 years of follow-up, a significant decline was found only in mean EPIC sexual summary scores. Prospective clinical studies are needed to determine the comparative effectiveness of PT and other radiation treatment strategies.

PMID: 27084658 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):386-95.

Proton Beam Reirradiation for Recurrent Head and Neck Cancer: Multi-institutional Report on Feasibility and Early Outcomes.

Romesser PB, Cahlon O, Scher ED, Hug EB, Sine K, DeSelm C, Fox JL, Mah D, Garg MK, Han-Chih Chang J, Lee NY.

PURPOSE: Reirradiation therapy (re-RT) is the only potentially curative treatment option for patients with locally recurrent head and neck cancer (HNC). Given the significant morbidity with head and neck re-RT, interest in proton beam radiation therapy (PBRT) has increased. We report the first multi-institutional clinical experience using curative-intent PBRT for re-RT in recurrent HNC. METHODS AND MATERIALS: A retrospective analysis of ongoing prospective data registries from 2 hybrid community practice and academic proton centers was conducted. Patients with recurrent HNC who underwent at least 1 prior course of definitive-intent external beam radiation therapy (RT) were included. Acute and late toxicities were assessed with the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 and the Radiation Therapy Oncology Group late radiation morbidity scoring system, respectively. The cumulative incidence of locoregional failure was calculated with death as a competing risk. The actuarial 12-month freedom-from-distant metastasis and overall survival rates were calculated with the Kaplan-Meier method. RESULTS: Ninety-two consecutive patients were treated with curative-intent re-RT with PBRT between 2011 and 2014. Median follow-up among surviving patients was 13.3 months and among all patients was 10.4 months. The median time between

last RT and PBRT was 34.4 months. There were 76 patients with 1 prior RT course and 16 with 2 or more courses. The median PBRT dose was 60.6 Gy (relative biological effectiveness, [RBE]). Eighty-five percent of patients underwent prior HNC RT for an oropharynx primary, and 39% underwent salvage surgery before re-RT. The cumulative incidence of locoregional failure at 12 months, with death as a competing risk, was 25.1%. The actuarial 12-month freedom-from-distant metastasis and overall survival rates were 84.0% and 65.2%, respectively. Acute toxicities of grade 3 or greater included mucositis (9.9%), dysphagia (9.1%), esophagitis (9.1%), and dermatitis (3.3%). There was 1 death during PBRT due to disease progression. Grade 3 or greater late skin and dysphagia toxicities were noted in 6 patients (8.7%) and 4 patients (7.1%), respectively. Two patients had grade 5 toxicity due to treatment-related bleeding. CONCLUSIONS: Proton beam re-RT of the head and neck can provide effective tumor control with acceptable acute and late toxicity profiles likely because of the decreased dose to the surrounding normal, albeit previously irradiated, tissue, although longer follow-up is needed to confirm these findings.

PMCID: PMC4997784 [Available on 2017-05-01]
PMID: 27084656 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):360-7

Clinical Outcomes and Patterns of Disease Recurrence After Intensity Modulated Proton Therapy for Oropharyngeal Squamous Carcinoma.

Gunn GB, Blanchard P, Garden AS, Zhu XR, Fuller CD, Mohamed AS, Morrison WH, Phan J, Beadle BM, Skinner HD, Sturgis EM, Kies MS, Hutcheson KA, Rosenthal DI, Mohan R, Gillin MT, Frank SJ.

PURPOSE: A single-institution prospective study was conducted to assess disease control and toxicity of proton therapy for patients with head and neck cancer. METHODS AND MATERIALS: Disease control, toxicity, functional outcomes, and patterns of failure for the initial cohort of patients with oropharyngeal squamous carcinoma (OPC) treated with intensity modulated proton therapy (IMPT) were prospectively collected in 2 registry studies at a single institution. Locoregional failures were analyzed by using deformable image registration. RESULTS: Fifty patients with OPC treated from March 3, 2011, to July 2014 formed the cohort. Eighty-four percent were male, 50% had never smoked, 98% had stage III/IV disease, 64% received concurrent therapy, and 35% received induction chemotherapy. Forty-four of 45 tumors (98%) tested for p16 were positive. All patients received IMPT (multifield optimization to n=46; single-field optimization to n=4). No Common Terminology Criteria for Adverse Events grade 4 or 5

toxicities were observed. The most common grade 3 toxicities were acute mucositis in 58% of patients and late dysphagia in 12%. Eleven patients had a gastrostomy (feeding) tube placed during therapy, but none had a feeding tube at last follow-up. At a median follow-up time of 29 months, 5 patients had disease recurrence: local in 1, local and regional in 1, regional in 2, and distant in 1. The 2-year actuarial overall and progression-free survival rates were 94.5% and 88.6%. CONCLUSIONS: The oncologic, toxicity, and functional outcomes after IMPT for OPC are encouraging and provide the basis for ongoing and future clinical studies.

PMID: 27084653 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):297-303.

A Prospective Outcomes Study of Proton Therapy for Chordomas and Chondrosarcomas of the Spine.

Indelicato DJ, Rotondo RL, Begosh-Mayne D, Scarborough MT, Gibbs CP, Morris CG, Mendenhall WM.

PURPOSE: To evaluate the effectiveness of definitive or adjuvant external beam proton therapy on survival in patients with chordomas and chondrosarcomas of the spine. METHODS AND MATERIALS: Between March 2007 and May 2013, 51 patients with a median age of 58 years (range, 22-83 years) with chordoma (n=34) or chondrosarcomas (n=17) of the sacrum (n=21), the cervical spine (n=20), and the thoracolumbar spine (n=10) were treated with external beam proton therapy to a median dose of 70.2 Gy(RBE) [range, 64.2-75.6 Gy(RBE)] at our institution. Distant metastases, overall survival, cause-specific survival, local control, and disease-free survival were calculated. RESULTS: The mean follow-up time was 3.7 years (range, 0.3-7.7 years). Across all time points, 25 patients experienced disease recurrence: 18 local recurrences, 6 local and distant recurrences, and 1 distant metastasis. The 4-year rates of overall survival and cause-specific survival were 72%; disease-free survival was 57%, local control was 58%, and freedom from distant metastases was 86%. The median time to local progression was 1.7 years (range, 0.2-6.0 years), and the median time to distant progression was 1.6 years (range, 0.2-6.0 years). The risk factors for local recurrence were age ≤58 years (62% vs 26%; P=.04) and recurrence after prior surgery (29% vs 81%; P=.01). Secondary cancers developed in 2 patients: B-cell lymphoma 5.5 years after treatment and bladder cancer 2 years after treatment. We observed the following toxicities: sacral soft tissue necrosis requiring surgery (n=2), T1 vertebral fracture requiring fusion surgery (n=1), chronic urinary tract infections (n=1), surgery for necrotic bone cyst (n=1), and grade 2 bilateral radiation nephritis (n=1). CONCLUSION: High-dose proton therapy controls more than half of spinal chordomas

and chondrosarcomas and compares favorably with historic photon data. Local progression is the dominant mode of treatment failure and may be reduced by treating patients at the time of initial diagnosis. The impact of age is a novel finding of this study.

PMID: 27084648 [PubMed - indexed for MEDLINE]

Int J Radiat Oncol Biol Phys. 2016 May 1;95(1):465-71.

Proton Therapy as Salvage Treatment for Local Relapse of Prostate Cancer Following Cryosurgery or High-Intensity Focused Ultrasound.

Holtzman AL, Hoppe BS, Letter HP, Bryant C, Nichols RC, Henderson RH, Mendenhall WM, Morris CG, Williams CR, Li Z, Mendenhall NP.

PURPOSE: Local recurrence of prostate cancer after cryosurgery (CS) and high-intensity focused ultrasound (HIFU) is an emerging problem for which optimal management is unknown. Proton therapy (PT) may offer advantages over other local therapeutic options. This article reviews a single institution's experience using PT for salvage of local recurrent disease after HIFU or CS. METHODS AND MATERIALS: We reviewed the medical records of 21 consecutive patients treated with salvage PT following a local recurrence of prostate cancer after CS (n=12) or HIFU (n=9) between January 2007 and July 2014. Patients were treated to a median dose of 74 Gy(relative biological effectiveness [RBE]; range: 74-82 Gy[RBE]) and 8 patients received androgen deprivation therapy with radiation therapy. Patients were evaluated for quality of life (QOL) by using the Expanded Prostate Index Composite questionnaire and toxicity by using Common Terminology Criteria for Adverse Events, version 3.0, weekly during treatment, every 6 months for 2 years after treatment, and then annually. RESULTS: Median follow-up was 37 months (range: 6-95 months). The 3-year biochemical progression-free survival (bPFS) rate was 77%. The 3-year grade 3 toxicity rate was 17%; however, 2 of these patients had pre-existing grade 3 GU toxicities from their HIFU/CRYO prior to PT. At 1 year, bowel summary, urinary incontinence, and urinary obstructive QOL scores declined, but only the bowel QOL score at 12 months met the minimally important difference threshold. CONCLUSIONS: PT achieved a high rate of bPFS with acceptable toxicity and minimal changes in QOL scores compared with baseline pre-PT functions. Although most patients have done fairly well, the study size is small, follow-up is short, and early results suggest that outcomes with PT for salvage after HIFU or CS failure are inferior to outcomes with PT given in the de novo setting with respect to disease control, toxicity, and QOL.

PMID: 26883560 [PubMed - indexed for MEDLINE]

Cancer Treat Rev. 2016 Feb;43:104-12.

Proton beams in cancer treatments: Clinical outcomes and dosimetric comparisons with photon therapy.

Doyen J, Falk AT, Floquet V, Hérault J(1), Hannoun-Lévi JM(2).

PURPOSE: To review current evidence of the role of proton therapy (PT) in other tumors than skull base, sinusal/parasinusal, spinal and pediatric tumors; to determine medico-economic aspects raised by PT. MATERIAL AND METHODS: A systematic review on Medline was performed with the following keywords: proton therapy, proton beam, protontherapy, cancer; publications with comparison between PT and photon-therapy were also selected. RESULTS: In silico studies have shown superiority (better dose delivery to the target and/or to organs at risk) of PT toward photon-therapy in most of thoracic and abdominal malignant tumors. Potential benefits of PT could be: reduction of toxicities (including radiation-induced cancer), increase of tumor control through a dose-escalation approach, hypofractionation. Cost of treatment is always cited as an issue which actually can be managed by a precise patient selection making PT a cost-effective procedure. Comparison plan with photon therapy may be useful to determine the dosimetric and clinical advantages of PT (Normal Tissue Complications Probability). CONCLUSION: PT may be associated with a great advantage compared to the best photon-therapies in various types of cancers. Accumulation of clinical data is on-going and will challenge the in silico data analysis. Some indications are associated with strong superiority of PT and may be discussed as a new standard within prospective observational studies.

PMID: 26827698 [PubMed - indexed for MEDLINE]

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A Phase 2 Trial of Concurrent Chemotherapy and Proton Therapy for Stage III Non-Small Cell Lung Cancer: Results and Reflections Following Early Closure of a Single-Institution Study.

Hoppe BS, Henderson R, Pham D, Cury JD, Bajwa A, Morris CG, D'Agostino H Jr, Flampouri S, Huh S, Li Z, McCook B, Nichols RC Jr.

PURPOSE: Proton therapy has been shown to reduce radiation dose to organs at risk (OAR) and could be used to safely escalate the radiation dose. We analyzed outcomes in a group of

phase 2 study patients treated with dose-escalated proton therapy with concurrent chemotherapy for stage 3 non-small cell lung cancer (NSCLC). METHODS AND MATERIALS: From 2009 through 2013, LU02, a phase 2 trial of proton therapy delivering 74 to 80 Gy at 2 Gy/fraction with concurrent chemotherapy for stage 3 NSCLC, was opened to accrual at our institution. Due to slow accrual and competing trials, the study was closed after just 14 patients (stage IIIA, 9 patients; stage IIIB, 5 patients) were accrued over 4 years. During that same time period, 55 additional stage III patients were treated with high-dose proton therapy, including 7 in multi-institutional proton clinical trials, 4 not enrolled due to physician preference, and 44 who were ineligible based on strict entry criteria. An unknown number of patients were ineligible for enrollment due to insurance coverage issues and thus were treated with photon radiation. Median follow-up of surviving patients was 52 months. RESULTS: Two-year overall survival and progression-free survival rates were 57% and 25%, respectively. Median lengths of overall survival and progression-free survival were 33 months and 14 months, respectively. There were no acute grade 3 toxicities related to proton therapy. Late grade 3 gastrointestinal toxicity and pulmonary toxicity each occurred in 1 patient. CONCLUSIONS: Dose-escalated proton therapy with concurrent chemotherapy was well tolerated with encouraging results among a small cohort of patients. Unfortunately, single-institution proton studies may be difficult to accrue and consideration for pragmatic and/or multicenter trial design should be considered when developing future proton clinical trials.

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New frontiers in proton therapy: applications in breast cancer.

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PURPOSE OF REVIEW: The aim of this article is to review published data on proton therapy in the multimodality treatment of breast cancer so as to provide an overview of the advantages and critical issues relating to this irradiation modality. RECENT FINDINGS: In-silico studies show a clear advantage in terms of dose homogeneity to the target and dose reduction to the non-target structures including heart, lungs, and healthy breast tissues. Clinical studies have shown the feasibility of proton therapy in breast cancer and allowed optimizing the technique by using multiple beams and intensity modulation. SUMMARY: Proton therapy is able to optimize the dose to the target and to reduce the irradiation of the healthy tissues. Clinical studies are expected to show a decreased risk of late side effects with potential improvement of the quality of life of breast cancer patients.

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