Second Belgian multidisciplinary meeting on urological cancers held in Brussels – March 28th, 2015

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Due to the success of last year, a second national Belgian multidisciplinary scientific meeting on urological cancers was held with the cooperation of medical oncologists (BSMO), urologists (BAU) and radiation oncologists (ABRO/BVRO). It was a great opportunity to build bridges between these three important specialisations involved in the treatment of urological cancers.

The steering committee of the meeting consisted of J. P. Machiels, G. Pelgrims, S. Rottey (members of BSMO); L. Hoekx, S. Joniau, T. Roumeguere (members of BAU); O. De Hertogh, G. De Meerleer and Y. Neybuch (members of ABRO/BVRO). The second meeting, held in Brussels on March 28th, 2015 was a great success with more than 100 attendees of the different specialisations involved.

In this meeting report you will find summaries of the lectures of Dr De Visschere (Radiologist) and Dr Schrijvers (Medical Oncologist).

(Belg J Med Oncol 2015;9(3):113-16)

Do's and don'ts in imaging in uro-oncology

There is a wide range of currently available advanced medical imaging techniques and they are rapidly evolving. As a consequence, clinicians sometimes struggle with the choice of the most accurate imaging technique to solve a given clinical problem. In uro-oncology, one of the most frequent questions is when to choose computed tomography (CT) and when to opt for magnetic resonance imaging (MRI). Traditionally, CT is considered the imaging technique of first choice, but MRI has superior soft tissue contrast and avoids radiation exposure. A whole abdominal MRI may indeed be a good alternative to CT for the detection of enlarged retroperitoneal lymph nodes, with comparable diagnostic accuracy, e.g. in the follow-up of young male patients treated for testicular cancer.[1] For the evaluation of renal or adrenal laesions, the accuracy of CT and MRI is equivalent but MRI suffers more often from motion and breathing artefacts. Therefore, CT is usually preferred for imaging of the upper abdomen and MRI for imaging of the pelvis, e.g. local bladder cancer staging or prostate cancer detection (*Figure 1a*). To help clinicians find their way among different imaging techniques, the Belgian government has developed imaging guidelines for a wide variety of clinical conditions.[2]

Most prostate cancers are detected based on serum-PSA elevation or suspicious digital rectal examination, followed by histological confirmation with systematic transrectal ultrasound (TRUS) guided biopsy.[3] The problem with TRUS-guided biopsy is sampling error: 30-40% of prostate biopsies are false negative, especially in the case of anterior tumours.[4] Imaging-based localisation of the tumour, however, improves the biopsy yield. For a good quality prostate MRI, a multiparametric approach is

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Conflict of interest: The authors have nothing to disclose and indicate no potential conflict of interest.

Keywords: imaging, renal cell cancer, uro-oncology.

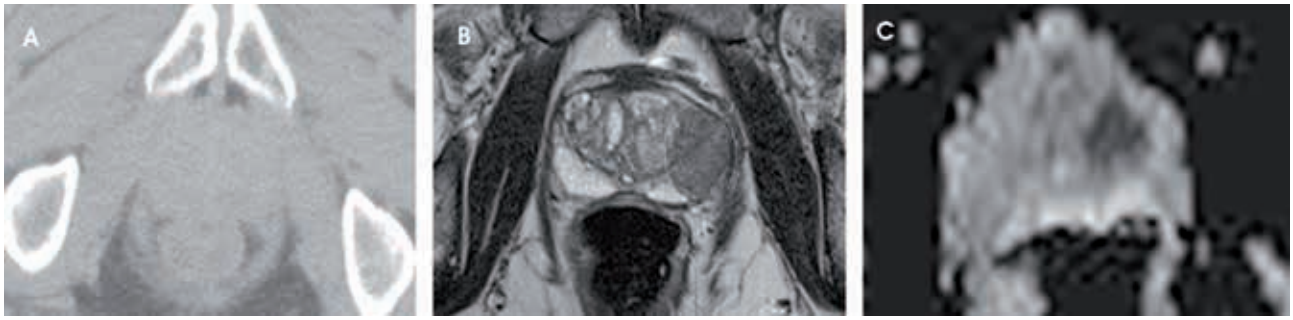

Figure 1. A 75-year old man with Gleason 4+5 prostate cancer on the left side of the prostate. On axial computed tomography (a), the prostate is homogenously grey and the tumour cannot be demonstrated. The prostate contour is difficult to discriminate from the rectum and pelvic musculature. With magnetic resonance imaging, on the morphological T2-weighted images (b) at the same level as (a) the prostatic anatomy is depicted and the high grade prostate cancer is visible laterally in the left prostate half as a homogenously low-signal intensity area (white oval). On diffusion-weighted images the tumour typically shows low signal intensity on the apparent diffusion coefficient map (c).

recommended, consisting of morphological T2-weighted images (*Figure 1b*), supplemented with functional imaging techniques such as diffusion-weighted imaging (*Figure 1c*), dynamic contrast enhanced imaging and/or magnetic resonance spectroscopy.[5] Multiparametric MRI (mpMRI) has excellent sensitivity for detecting aggressive Gleason ≥7 cancers.[6] The detection rates depend on the Gleason grade and size of the tumour, ranging from 21-29% for <0,5 cc tumours with Gleason ≤6 to 100% for tumours >2cc with Gleason ≥8.[7] A recently published systematic review on the question whether mpMRI can detect clinically significant prostate cancer, reported accuracies of 44-87%, sensitivities of 58-97% and specificities of 23-87% with trends depending highly on the definition of clinically significant disease.[8] In patients presenting with elevated PSA, mpMRI may be used before prostate biopsy, to allow (only) targeted biopsy to a suspicious lesion detected on mpMRI, or to avoid immediate biopsy in the absence of any suspicious lesion.[9] As compared to standard random TRUS biopsy, an equivalent detection of clinically significant prostate cancer is achieved (43%), using fewer biopsies (only 3.8 cores versus 12 standard) in one third fewer men, resulting in a 10% reduction in the diagnosis of clinically insignificant prostate cancer.[10] MpMRI may also help select the best candidates for active surveillance, as visible cancer on mpMRI is a predictor of unfavourable disease.[11]

Highlights of ASCO GU: Renal cell cancer (RCC)

The classification of renal cell cancer (RCC) was until recently made by histological characteristics and renal cancers were categorised as clear cell cancer (75% of all RCC); papillary type 1 and 2 (respectively 5-10%), chromophobe (5%) and oncocytoma (5%).[12]

Based on The Cancer Genome Atlas (TCGA) Research Network, different molecular subtypes based on mRNA and miRNA in clear cell RCC with different prognosis have been described.[13] Genetic testing will have implications in the classification of RCC in the future.

Localised disease

The risk of recurrence of RCC after surgery is classified according to clinical parameters related to the patient and tumour characteristics; and different risk scoring systems have been used (e.g. UCLA International Staging system (UISS)). Genetic testing is being evaluated to predict recurrence and even in patients with a low risk of recurrence, different risk groups can be defined based on genomic expression with recurrence rates from 2-23% in stage I disease.[14]

The ASSURE trial assessed the value of adjuvant treatment in patients with a high-risk RCC and treated them for one year with placebo, sunitinib or sorafenib. The primary endpoint was disease-free survival (DFS) and secondary endpoints were overall survival (OS), side effects and biomarker analysis. The study accrued 1,943 patients with non-metastatic RCC, which had resectable disease by CT-scanning and with >T1bNany (resectable) M0 disease. After surgery, patients were stratified according to the risk, histology, performance status and type of surgery. Patients were randomised to placebo, sunitinib (50 mg/day q4/6 weeks for nine cycles) or sorafenib (2 x 400 mg/day for one year).

There was no difference in DFS (HR sunitinib = 1.01; HR sorafenib = 1.0) with 5-year DFS rates of 53.8% for

placebo, 55.8% for sunitinib and 52.8% for sorafenib and median DFS of 6.0 years for placebo and 5.8 years for both sunitinib and sorafenib. There was also no difference in OS.

The authors concluded that this was a negative study and that in patients with locally advanced, resected high-risk RCC, adjuvant treatment with sorafenib or sunitinib is not indicated.[15]

Metastatic disease

The prognosis of patients with metastatic RCC (mRCC) was historically determined by Motzer et al.[16] In late 2000, Heng et al. defined another prognostic system applicable in patients treated with targeted therapies that could better differentiate among prognostic groups.[17] During the ASCO GU, new different prognostic criteria were discussed.

First was the neutrophil to lymphocytes ratio (NLR). Neutrophils are a major component of cancer-related local inflammation stimulating the tumorigenic microenvironment whereas lymphocytes are suppressors of cancer progression and are an independent predictor of survival in RCC patients. In this study, the prognostic role of NLR and NLR conversion on PFS and OS was studied in 5,227 patients with mRCC and treated with targeted therapy. The authors looked at the NLR at initiation of first-line targeted therapy and at six weeks after start of treatment. They proved that the median survival in patients with a NLR <3 was better than in patients with a NLR >3 (26.7 versus 12.4 months, HR = 1.47, p<0.001). Also, when the ratio of NLR decreased from >3 to <3 at weeks six after the start of treatment, the OS was better in these patients (21.4 versus 9.7 months, HR = 0.56); while in patients in whom the NLR ratio increased, OS was worse than when it stayed below 3 (14.3 versus 30.0 months, HR = 2.0).[18]

Another prognostic factor is the body mass index (BMI). In a retrospective study including 4,657 patients with metastatic RCC and treated in phase II-III clinical trials, the impact of the BMI on OS, PFS and ORR were determined as was the impact of fatty acid synthase (FASN) expression on these outcome parameters. There was a positive impact of a BMI higher or equal to 25 compared to those with a lower BMI on overall response rate (25.3 versus 17.3%), PFS (8.2 versus 5.5 months) and OS (23.4 versus 14.5 months). A high BMI was associated with a low FASN expression and FASN expression was associated with a lower OS (27.5 versus 14.5 months).[19]

Another possibility to determine the prognosis of patients with RCC is by use of The Cancer Genome Atlas, which is a project to comprehensively characterise the genomic and molecular features of different cancer types. The authors wanted to stratify patients with a clear cell carcinoma based on a genomic profile determined by TCGA reverse phase protein array. They could identify five clusters and two clusters were associated with a worse or better prognosis. The cluster with a poor prognosis was linked to a decreased expression of receptor tyrosine kinases (RTK); an upregulation of the mTOR pathway; mTOR pathway genomic alterations; sarcomatoid histology; and a clear cell prognostic mRNA signature, while patients with a good prognosis had an increased expression of RTKs and a downregulation of the mTOR pathway.[20]

Conclusion

Do's and don'ts in imaging in uro-oncology:

In conclusion, CT is generally the preferred imaging technique for the upper abdomen in uro-oncological imaging, although MRI may be a good alternative. In the pelvis, MRI is superior to CT, for example in bladder cancer staging or prostate cancer detection. For the latter, a multiparametric MRI is recommended, and it should be used to detect or exclude high grade or large prostate cancers, rather than any prostate cancer.

Highlights of ASCO GU: Renal cell cancer (RCC):

To date, data show no benefit for the use of adjuvant treatment in patients with a high risk renal cell cancer. RCC seems to be a heterogeneous disease and better biomarkers are urgently needed to differentiate the prognosis of these patients and guide treatment decisions. An ideal biomarker should have an expression that is significantly related to the disease; be readily quantifiable in accessible biological or clinical samples; economical, quick, and consistent; and correlate with a specific outcome.

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