

Hein Van Poppel:

Urological cancer is what we do

→ Marc Beishon

Hein Van Poppel, director of the European School of Urology, is driving forward the training and accreditation of Europe's urological oncologists. He wants to see an end to untrained urologists dishing out cancer medicines – but he is no more keen on medical oncologists who treat kidneys, prostates and bladders without any specialist training in these organs.

People working in cancer often look back over the last few decades and see an era of enormous progress in understanding and treating the many oncological diseases. But there are other medical fields that have seen equally remarkable progress, none more so than urology, which in just 25 years has developed from a minor surgical specialty into a major, complex surgical and medical discipline with a number of 'super-specialties', including neurological, female, paediatric and reconstructive urology, and of course oncological urology.

And it is oncological urology that is very much at the centre of the debate on the delivery of cancer treatment in Europe, in particular the arguments between specialists who practice medical oncology and the movement to bring more specialties into a common oncology 'society'. For Hein Van Poppel, chair of the department of urology at the Catholic University Hospital in Leuven, Belgium, and a leading light in all manner of urology and oncology organisations, the issue is straightforward.

"Urologists are different to other specialists such as gastro-enterologists and abdominal surgeons. We do everything for the patient, from diagnosis through to surgery, medical treatment and end-of-life care. We

have delivered treatments such as hormonal drugs for years and there is no reason not to administer cytotoxic and newer targeted therapies, as we know the urological malignancies of our patients much better than many medical oncologists. How can they be a specialist in the treatment of all different organ cancers just because they have tools such as cytotoxic therapies that are difficult to manage? The tool does not allow you to master the organ – that is an error in the mind of many medical oncologists. It is more important to know the patient than to know the drug."

The proviso – and it is a hugely important one – is that such care must be delivered by trained and preferably accredited oncological urologists, ideally in a multidisciplinary setting. In academic centres such as at Leuven, that expertise is a given, and as Van Poppel adds, "In fact, it is not important who delivers the therapy indicated in multidisciplinary discussions. It could be the urologist or medical or radiation oncologist, as long as they can deliver a drug with the same pertinence and safety."

Belgium, says Van Poppel, is now taking a lead in Europe in developing an oncological accreditation for urologists that allows them, just like medical oncologists, to prescribe and administer medical cancer treatments. He points also to new initiatives that are



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building bridges between the oncology specialties. In Barcelona this year, the European School of Urology held its second masterclass on medical treatment of urological malignancies, sponsored by the European Association of Urology (EAU). From next year this masterclass will also be open to medical oncologists and other cancer specialists. Then in November, also in Barcelona, the first European Multidisciplinary Meeting on Urological Cancers will be held, with “for the first time in history”, the EAU, ESMO (European Society for Medical Oncology) and ESTRO (European Society for Therapeutic Radiology and Oncology) joining urological forces to focus, in this event, on prostate and kidney cancers.

Van Poppel is heavily involved in such training and education. He is director of the European School of Urology, the education office of the EAU – “This,

together with membership of the ESMO faculty, is the most important of all my international roles.” Flagship masterclass and resident training programmes for all urologists in Europe, in addition to the new oncology events and the growing influence of the EAU’s annual congress, all contribute to making urology one of the most powerful and high-profile disciplines in Europe – closely rivalling cardiology, he reckons.

“The multidisciplinary meeting on urological cancers is especially important politically for European urology. I believe we can deliver education that is at least as good as the one offered by other societies in the US. I have 150 teachers in the European School of Urology faculty and 40% are oncology experts.”

On the cancer side he is also, naturally, active in the European Society of Surgical Oncology (ESSO), and the European Organisation for the Research and

State-of-the-art.
Van Poppel with the latest addition to his oncology department – an impressive piece of robotic technology that surgeons can use to improve precision, stability and dexterity

“It is more important to know the patient than the drug”

Treatment of Cancer (EORTC). During his career at Leuven he has developed local expertise in radical prostatectomy and partial nephrectomy and bladder replacement, while also leading landmark international research on both techniques.

The rigour and breadth of Van Poppel's oncological experience is impressive, and he is more than qualified to turn the call for organ-based specialism onto medical oncologists themselves. "Medical oncologists have an almost exclusively pharmacological approach to cancer, based on its own physiology. But cancer is a disease of organs and is much more than physiology. It is a complex disease involving many aspects of the human being including symptoms and side-effects. Urological oncologists are organ driven, and able to see the complexity of the tumour and apply oncologic surgery and radiotherapy, and use different drugs. Many radiation oncologists have for some years dedicated themselves to certain organs and we have uro-radiation oncologists who belong specifically to our care programme. All I ask is that

medical oncologists know as much about urological diseases as we do – and that really means being dedicated to certain organs as we are."

A Belgian from the Flemish side of the country, Van Poppel trained for three years at the French-speaking Namur University before completing medical school at Leuven, gravitating to surgery in his final year. "I believed I could do more for patients with surgery, and was set for a career in general work at a community hospital until I was asked if I wanted an academic appointment at Leuven's urology department. The dean of the faculty of medicine sent me abroad for two years and, although I was working on a thesis on neurogenic bladder, I met, among others, oncology specialists Fritz Schroeder in Rotterdam and Rudolf Hohenfellner in Mainz. They convinced me their field held the most interest." He also gained much experience as a pupil of the famous Barcelona-based surgeon José-Maria Gil-Vernet – still a close contact.

He returned to Leuven, finished his thesis, but moved on to specialise in oncological urology,

Committed to education. Van Poppel with faculty member Joaquim Bellmunt, at the second ESU masterclass on medical oncology for urologists, held in Barcelona earlier this year



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gradually phasing out work in other subspecialties over the years. “Urology then really was the poor relation in surgery at Leuven and elsewhere – we were just doing foreskins, transurethral operations and so on. I totally disagreed that after doing a couple of years of general surgery and some endoscopy you became a urologist, with the ‘big surgery’ such as nephrectomies handed to other surgeons. We felt pushed in a corner – and we pushed back, and have been ever since.”

Following the lead of surgeons such as Schroeder, who came back from the US to introduce radical prostatectomy, the technique that should, in the right hands, spare functions such as continence and potency for certain grades of tumour, Van Poppel and colleagues transformed their department to one that handles all major urological surgery and treatment. In 2002 he became department head, adopting a policy of giving colleagues their head to develop other key specialties, while he focused on oncology.

“This has been tremendously successful – I’ve seen other units where the chief tries to keep on top of everything and it just doesn’t work. We need specialists who can develop their own care, teaching and research programmes. The surgeon who is very good at endoscopic transurethral resections of the prostate is probably not the best to do extensive lymph node dissections after chemotherapy – it’s a different type of surgery.”

The development of specialisms across the five main pillars of urology, as he calls them – paediatric, functional, reconstructive, endourology and oncology – did need some careful guidance on his part, and a particular aim was to bring the unit to international attention. That has been achieved with a focus on state-of-the-art surgery and leading and participating in key research topics, such as radical prostatectomy on the oncology side.

Working conditions have also improved greatly. The urology unit moved from an old hospital in central Leuven to join a huge modern site called Gasthuisberg on the edge of the city (despite its small size, the city of Leuven has long been competing with Brussels as the

Belgian capital). This university hospital has some 1,800 beds and is a major centre in the Flanders region, also attracting patients from abroad. “We now have our own outpatient department and clinic for small operations across two floors of the hospital. We were able to convince the management that we were growing so fast we needed dedicated facilities.”

There is a large volume of urological work. “Each morning we discuss all hospitalised patients – there are more than 40 – and I run an outpatient clinic once a week for 30 people with often second/third opinion oncological problems. On days scheduled for oncology surgery we do two to four major cases – say four radical prostatectomies or two bladders. People have said we are crazy to do so many in one day, but if we don’t, we end up with a waiting list that’s too long.”

Leuven is a referral centre for difficult cases such as vena cava thrombus and salvage surgery after chemo- or radiotherapy, and also carries out operations that are not widely available in some other countries. “Take radical prostatectomy for locally advanced cancer – many urologists don’t do this, sticking to guidelines that in some countries recommend hormonal and radiation treatment. But when patients are clever, they find out about the success rates of surgery and ask for radical prostatectomy – and when they can’t get it they come here.” Men from Scandinavia are among those arriving at Leuven, he says.

“For patients with locally confined prostate cancer, I prefer to use the term ‘total prostatectomy’, as the word ‘radical’ makes men rather afraid,” he says. “It’s a marginal resection that preserves the neurovascular bundles and sphincter. Surgeons who tell their early prostate cancer patients they will lose their potency because they can’t do nerve sparing surgery need retraining.”

Van Poppel is certainly an authority on radical prostatectomy, having performed more than 1,800 operations himself. He has also introduced techniques such as robot-assisted laparoscopy, in place at Leuven for a few months now. But he is clear that quantity does not necessarily mean quality. In an

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evaluation of surgeons in EORTC’s genito-urinary group, he found that meeting higher quality parameters did not relate always to a higher caseload.

“A very high volume may not be better, because the surgeon may not find the work challenging enough or because he continues to make the same errors during every surgery. I believe oncological and urological outcomes are the only factors that should allow urologists to continue with this type of surgery. Analysing just a couple of parameters in 10 early prostate cancer operations can assess their surgical skill.”

Van Poppel set this out in a paper in the *European Journal of Cancer* in 2001, where duration of surgery, transfusion need, post-operative PSA (prostate specific antigen), status of the surgical margins and incontinence were assessed. “A certain volume of procedures is probably needed to gain and keep experience, and maybe 25 to 40 procedures a year per surgeon is optimal.” This was also concluded in a recent presentation at the American Urological Association by a multi-centre European–Canadian study. But it may be a tall order to raise the bar across Europe for this operation, given that minimum case loads in some countries are as low as five.

Other research he highlights with the EORTC is a study he coordinated with Michel Bolla from Grenoble that showed the benefits of post-operative radiotherapy for high-risk prostate cancer patients. But perhaps his landmark work is performing some of the first series of partial nephrectomies in Europe (where only part of the kidney is removed) and an EORTC trial that he designed and coordinated of a prospective comparison of partial versus radical nephrectomy in low-grade renal carcinoma. “It has become obvious that nephron-sparing surgery decreases the possible occurrence of renal failure and the need for dialysis,

and this phase III study aimed to look at complication rates and oncological outcomes.” It involved more than 40 centres and was also opened to intergroup study in North America, although the latter could contribute only few patients, notes Van Poppel.

“It was closed prematurely because everyone was doing partials without waiting for the results. We are now doing the analysis and will publish in early 2008.”

Leuven is active in plenty of other research. “Dendritic cell vaccination treatments and microarray work for kidney cancer, photodynamic diagnosis with hypericin [an extract from St John’s wort] for superficial bladder cancer, choline PET-scan for sentinel lymph node investigation in prostate cancer and, even more importantly, chemoprevention trials for bladder and prostate cancers are all ongoing,” he notes. New minimally invasive treatment strategies with percutaneous radiofrequency ablation for kidney tumours and high-intensity focused ultrasound for prostate cancer are also being explored in prospective multi-centre studies. Overall, he and colleagues have a prodigious oncology research volume.

While much of Van Poppel’s research revolves around surgery, he is just as well up on the many new drug treatments, and was course director, with close friend Ziya Kirkali from Turkey, of the second Barcelona masterclass on medical oncology for urologists. This course had four modules – hormone and intervesical therapy, chemoprevention and immunotherapy, targeted therapy and cytotoxic chemotherapy – and there are many new approaches now in phase II and III studies. There was a European Board of Urology examination at the end, leading to a certificate that will be useful in the accreditation of urological oncologists, says Van Poppel. “The difficulty of the exam is high and, of the urologists taking it, younger ones did

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Off duty. Van Poppel enjoys a beer with his wife Conny and their three girls Ineke, Loesje and Ellen

better than older colleagues. By the way – Belgium was the best represented country on the course.”

Although practices differ around Europe, there are common patterns in who is delivering certain drug therapies. “Medical oncologists are only involved in part of the treatments for the malignancies we see. In most countries this is interferon for kidney cancer, and cytotoxic chemotherapy for bladder, testicular and penile cancer. Hormonal therapies for prostate cancer are given by urologists – we have long been approached by the drug companies to deliver these – and we can now deliver new treatments for kidney cancer.”

The key is of course multidisciplinary consultation, with all participants increasingly dedicated to urology, which Van Poppel recognises will be very difficult in smaller hospitals. But clearly the path he is set on is for urologists to involve themselves more in all aspects of care, in the absence of commitment from medical oncologists (who, to be fair, he says are not present in enough numbers in most European countries). “But every patient with an oncological problem should have the right to have his case extensively discussed by all the specialists involved in the

diagnosis, the staging and the treatment of his disease.”

What must be policed, however, are urologists in outlying clinics who think they can prescribe drugs, say for metastatic prostate cancer, while practising as an everyday all-round urologist. Only two years of supplementary oncology training for newcomers, and rigorous accreditation at the likes of the ESU’s masterclasses, and by country agencies, will do, he says.

Equally, medical oncologists must recognise, he adds, the danger in prescribing treatments for say metastatic renal carcinoma without discussing the case with the urologist and other surgeons, as surgical intervention may offer a better chance, say for a pulmonary metastasis. “Medical oncologists who attend our masterclasses will learn about this and other topics, such as knowing you have to stop drug therapy at a certain stage in superficial bladder cancers and perform a cystectomy,” he says.

It all boils down to who knows the treatments – and the patients – the best, and if he could, Van Poppel would also reverse the trend for specialist palliative care units and let patients remain in the hands of their primary physician.

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When it comes to his most broad interest, Van Poppel's focus is firmly on prostate cancer and the entire life cycle of the disease, including its possible prevention. “Most of the research so far on green tea, lycopene, vitamin E and so on has been badly done, but it is important we find out if there is something we can offer men, especially those with a family history of prostate cancer. Chinese men have as much PIN [prostate intraepithelial neoplasia, or carcinoma in situ] as men in the West, but ten times less invasive cancer. The only way to investigate is through randomised trials in high-grade PIN patients. We have done this with soy, vitamin E and selenium, and are now doing it with lycopene, and we will move on to other agents.”

Treatment guidelines for the various cancer stages and ages are also a big concern, especially as overtreatment is a common problem – and conversely, adopting an ‘active surveillance’ approach may mean a

window for optimal treatment may be missed. A critical age group is younger men aged 50–65 – as Van Poppel says, if you find a small cancer in a 50 year old and carry on with surveillance, noting rising PSA levels, how long do you wait?

“With a Gleason score of 6 [where cancer cells are moderately differentiated], you can have a radical prostatectomy, where the only drawback of the surgery should be loss of fertility. But if you wait, many men will suffer years of anxiety, and you risk a more extensive operation with less chance of a cure.” He notes the difficulty of recruiting younger men into active surveillance trials, where the end point is time to metastasis, and which also involve biopsies and attendant risks. “I don't think this should be encouraged. With a Gleason score of 6 or 7 and a PSA of less than 2.5 you still can't cure all cancers with radical prostatectomy. You and the patient are taking a risk by waiting.”

Other urologists, in particular Laurence Klotz in Toronto, are promoting delayed radical intervention through active surveillance as the best balance in the over/undertreatment debate. Men who have had radical treatment can also suffer as much anxiety (about cancer recurrence) as those on watchful waiting. In the other camp are other top urologists such as Bill Catalona and Van Poppel, favouring earlier radical prostatectomy. It is currently the only treatment for localised prostate cancer that has shown a cancer-specific survival benefit when compared to conservative management in a prospective, randomised Scandinavian trial. “Early surgery will allow the patient to recover urinary and sexual function with a very high likelihood of definitive cancer cure,” he says.

It is only men aged 65 and over who are offered curative radiation therapy in the Flanders region covered by Leuven, except in exceptional circumstances. “If you're below 65 and approach our radiation oncologists for treatment, such as external beam or interstitial radiotherapy, they will refer you to me,” he says. “It's not just that there is less chance of a

With Mr Cisplatin. Lawrence Einhorn (right) developed the breakthrough treatment for testicular cancer



cure, but salvage surgery can be very difficult. But above 65 the impact of surgery on quality of life is greater and survival is comparable." Above 75, hormonal therapy is sometimes more than enough to allow the patient to reach his normal life expectancy without ever suffering any cancer symptom.

What does concern Van Poppel is that the best management is only possible in centres where the widest choice of treatments is available. Leuven has open and laparoscopic (now robot-assisted) surgery, radiotherapy (including brachytherapy), and high-intensity focused ultrasound and IGRT (image-guided, intensity-modulated radiotherapy). "The only one we don't have is cryotherapy (freezing therapy). Patients need an honest opinion on what is best for them – but there are specialists whose salaries are linked to certain treatments and they will convince the patient that their modality is best."

Like many *Cancer World* interviewees, Van Poppel is particularly critical of overtreatment, mentioning that radical treatment is being offered to men with the carcinoma in situ condition (PIN), who are genuine candidates for watchful waiting, since they have no invasive carcinoma. And brachytherapy is one curative treatment option where patients and doctors may be jumping on fashion. "Propaganda on the Internet is certainly to blame, and I feel it is often given to men who probably don't need treatment at all." It's also a treatment that, like radical prostatectomy, can be performed badly, he adds, and the decision is critical given that you only have one chance at the best treatment.

He says the best promoters of better treatment standards are undoubtedly patient groups, with Europa Uomo, the European Prostate Cancer Coalition, very much to the fore. Van Poppel is the advocacy organisation's scientific chairman, and says he is impressed by how much work has already been done in developing links with national groups since it was founded in 2002. "I give the board an update on prostate cancer at its general assembly, and it is a difficult talk, as they know more about it than some doctors," he says (slides of his latest talk are on Europa Uomo's website, which can be reached at www.cancerworld.org).

A priority is PSA testing, he says. "PSA testing first at age 40 and then at 45 and 50 – the age when men start to develop cancer – will help to show who is at risk of developing dangerous disease and who will need more strict follow-up. Patient groups will be much more effective at lobbying governments for more affordable PSA tests than doctors." Access to second opinions and countering inappropriate treatment are also priorities for patient coalitions such as Europa Uomo, he feels. "At Leuven, we held a recent event in which 300 patients discussed their experiences of living after radical prostatectomy," he adds.

Van Poppel plans to continue his clinical and teaching roles at Leuven, although he is envious of urologists who have their own research labs. "I'd like to run one like Fritz Schroeder's in Rotterdam and Frans Debruyne's in Nijmegen. I'm working on it. Prostate cancer research would be my priority."

Outside of Leuven, his aims are to continue to raise educational standards for urologists in Europe and further afield. "All European urologists should pass the European Board of Urology exams – it must be a minimum requirement" – and he is in favour of legal measures to compel continuing education.

Home life for Van Poppel is calmer now that his three daughters are grown up, although he and his wife Conny still organise family holidays – the latest to Barcelona, which just happened to be where ECCO, the congress of the European CanCer Organisation was taking place. On a personal note he talks of a recent case of cancer in his close family – despite working with cancer patients for many years this has really brought home to him just how important it is, as a doctor, to relate to people. When he has spare time he likes to play golf – just don't ask about his handicap.

The Leuven school of urology has a logo made up of a drawing of the male and female urological and the male genital organs by Philip Verheyen, a 17th century Flemish anatomist and surgeon at Leuven. Verheyen's mission – to understand underlying physiology before embarking on disease treatment – could hardly hold more true for Van Poppel and colleagues today.

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