Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg Study Group for Enhanced Prostate Diagnostics

Timur H. Kuru[1,2], Karan Wadhwa[6], Richard Tsung Meng Chang[8], Lina Maria Carmona Echeverria[10], Matthias Roethke[2], Alexander Polson[11], Giles Rottenberg[9], Brendan Koo[4], Edward M. Lawrence[4], Jonas Seidenader[1], Vincent Gnanapragasam[6], Richard Axell[7], Wilfried Roth[3], Anne Warren[5], Andrew Doble[6], Gordon Muir[10], Rick Popert[8], Heinz-Peter Schlemmer[2], Boris A. Hadaschik[1] and Christof Kastner[6]

[1]Department of Urology, University Hospital Heidelberg, [2]Department of Radiology, German Cancer Research Center (DKFZ), [3]Institute of Pathology, University of Heidelberg, Heidelberg, Germany, Departments of [4]Radiology, [5]Histopathology and [6]Urology, [7]Clinical Engineering, Cambridge University Hospitals, Cambridge, [8]Urology Centre, and [9]Department of Radiology, Guy's & St Thomas' NHS Foundation Trust, Guy's Hospital, [10]Department of Urology, Kings College Hospital, and [11]Department of Cellular Pathology, Guy's & St Thomas' NHS Foundation Trust, St Thomas' Hospital, London, UK

Timur H. Kuru and Karan Wadhwa contributed equally to the present study.

Objectives

- To define terms and processes and agree on a minimum dataset in relation to transperineal prostate biopsy procedures and enhanced prostate diagnostics.
- To identify the need for further evaluation and establish a collaborative research practice.

Patients and Methods

- A 19-member multidisciplinary panel rated 66 items for their appropriateness and their definition to be incorporated into the international databank using the Research and Development/University of California Los Angeles Appropriateness Method.
- The item list was developed from interviews conducted with healthcare professionals from urology, radiology, pathology and engineering.

Results

- The panel agreed on 56 items that were appropriate to be incorporated into a prospective database.
- In total, 10 items were uncertain and were omitted. These items were within the categories: definitions ($n = 2$), imaging ($n = 1$), surgical protocols ($n = 2$) and histology ($n = 5$).

Conclusions

- The components of a minimum dataset for transperineal prostate biopsy have been defined.
- This provides an opportunity for multicentre collaborative data analysis and technique development.
- The findings of the present study will facilitate prospective studies into the application and outcome of transperineal prostate biopsies.

Keywords

biopsy, consensus, dataset, standardization, template, transperineal

Introduction

Prostate cancer (PCa) is the most common solid tumour and the third leading cause of cancer death in men in developed countries [1]. There is a high variety in the incidence rates worldwide, which can partly be explained by differences in the use of PSA testing. One main burden of PSA testing, and especially screening, is that it detects

both aggressive tumours and indolent cancers. The reduction of PCa mortality by the use of PSA screening continues to be a matter of discussion, although a large European-based randomized trial identified a significant but modest benefit [2]. Even after 11 years of follow-up, the number needed to screen to prevent one PCa death is very high (at 1055 patients) and the number needed to treat is 37 patients [2]. This reaffirms why overdiagnosis and overtreatment need to be reduced, both from a medical and an economical point of view.

Although overdiagnosis will probably be reduced by incorporating image-guided biopsy approaches [3], overtreatment can be avoided through the use of active surveillance protocols for low-risk tumours. One of the key challenges for PCa therapy, and especially for the safe application of active surveillance, is how to best optimize the grading and organ-confined staging in respect of the volume of tumour lesions, aiming to avoid any mischaracterization of disease. Precise information about tumours is necessary to allow discussion of the appropriate treatment for each man with PCa.

Transperineal biopsies allow better access to the anterior prostate. Batura et al. [4] have reported the growing resistance of intestinal flora to antibiotics. In this respect, the transperineal technique may have added benefit over the transrectal approach for avoiding dislocation of bacteria into the prostate, potentially leading to decreased infection rates.

A possible solution for optimal transperineal staging was reported by Onik et al. [5] with respect to transperineal mapping biopsies. This technique improved local staging but had a high procedure-related morbidity and leads to economic issues concerning the capacity for pathology processing. Transperineal prostate biopsy techniques using a systematic distribution of smaller core numbers showed promising results in smaller cohorts, especially when restaging men under active surveillance [6]. Different techniques have been described with a different number and/or distribution of biopsies [7,8], although these vary greatly, making it difficult to compare outcomes. The reporting of MRI and histopathology also remains unstandardized, even within collaborating units.

Although the available literature suggests the superiority of the transperineal biopsy approach, several techniques have been described. The present study aimed to define terms and processes and agree on a minimum dataset in relation to transperineal prostate biopsy procedures. This will enable multicentre studies to obtain a better evidence base and more reliable, meaningful results from the analysis of transperineal biopsies and techniques.

Patients and Methods

A 19-member multidisciplinary panel rated 66 items for their appropriateness and definition to be incorporated into the international databank with help of the Research and Development/University of California Los Angeles Appropriateness Method (RAM) [9]. RAM is a combination of both the Delphi [10] and nominal group techniques [9]. It is a process for a structured group judgement incorporating expert clinical knowledge and the available literature. RAM has been used previously in a number of other areas, including coronary revascularization [11], cataract surgery [12] and prostatectomy [13]. In this consensus process, an expert panel rates items over two rounds. The first round was conducted by e-mail, collecting items of interest and relating statements. In the second round, the panel met to discuss their initial statements that were supported by pre-existing evidence from the available literature and then a second and final vote was cast. The item list was developed using interviews with healthcare professionals from urology, radiology, pathology and engineering.

The meeting convened at the University Hospital Heidelberg, Germany.

Panel Members

The panel comprised five consultant urologists, four consultant radiologists, two consultant pathologists, one engineer and seven residents in urology or radiology. The engineer had several years of experience in medical ultrasonography and image fusion. The panel members were drawn from academic teaching hospitals in Germany and the UK.

Constructing the Item List for the Consensus Process

The list of 66 items for discussion in the consensus process was developed over different stages.

First, semi-structured interviews were conducted by e-mail with experts in transperineal prostate biopsy. There were four main categories that were identified: (i) definitions, (ii) imaging, (iii) surgical protocol and (iv) histology. These main categories were subdivided into subcategories. The authors discussed these items during the consensus process.

The RAM Consensus Process

Items were individually assessed for their appropriateness to be incorporated into the database. Items were scored as 'appropriate', 'inappropriate' or 'uncertain'. The group's judgement was assessed by a show of hands. Only items rated as appropriate were considered to be suitable for incorporation into the document. During the consensus

Table 1 Summary of the areas of agreement and uncertainty.

Area	Number of topics for discussion	Appropriate, *n*(%)	Uncertain, *n*(%)
Definitions	22	20 (91)	2 (9)
Imaging	7	6 (86)	1 (14)
Surgery	25	23 (92)	2 (8)
Histology	12	7 (58)	5 (42)

meeting, items were discussed one by one, facilitated by changing chairs from different institutions. The chair ensured that every participant of the meeting had the opportunity to discuss each item. Participants had the opportunity to reconsider their appropriateness rating and change it before a final vote was made.

Results

Items with Agreement Reached

Overall, there were 66 topics considered for discussion, each with at least two definitions providing the items for the voting process. There was a trend towards agreement in all areas, with 56 definitions (85%) decided with 100% consensus of 16 or more members, as per the RAM criteria. A summary of the areas of agreement and uncertainty for each section is presented in Table 1. Table 2 summarizes the definitions with agreement, including a minimum and optimal requirement. These definitions are the formal outcome of the process indicating the state of practice in the study centres going forward.

Items with No Agreement or Uncertainty

Although there were no areas tht were deemed inappropriate, there were important areas where there was little or uncertain consensus. These are listed under their respective sub-section.

Definitions

The definition of maps was left as an uncertain area requiring further research. No clear definition could be reached and a statement for an optimal requirement ('a geographical representation of the prostate to allow communication') requires further clarification and is put forward as a point for research. As a starting point in this research, the descriptive maps of Dickinson et al. [14] were proposed for use in the minimum dataset.

Active surveillance is a contentious issue in the current practice of urology. Although the proposed definition ultimately reached consensus, with a RAM score of >16, there was some 'uncertainty' in the exact follow-up scheme in those protocols. Continual monitoring in a population of patients with localized PCa (with a view to curative intent) according to locally agreed pathways is the minimum requirement for this definition.

Imaging

The consensus group agreed that one main issue was attempting to standardize MRI image acquisition and target reporting with regard to PCa detection. The use of MRI for PCa detection has been discussed by two recent European consensus groups [14,15]. It was agreed that, as a standard of practice, information for each MRI target should be collected in a consistent and reproducible manner involving both localization of the target in the prostate and a 1–5 suspicion score. This allows for the proper support of biopsies involving MRI targeting and allows for feedback from pathology reports to the MRI reader for learning purposes.

It was also agreed that the process of transferring reporting information carries the risk of a loss of the original information: first, as the target information is transferred into a drawing or reporting form and, second, as it is cognitively transferred from drawing or report to live ultrasonographic-guided biopsy. This can be overcome by direct reporting by the radiologist onto an MRI image set, with eventual overlay of the image onto the live ultrasonographic image by fusion software, although the most common fusion techniques still carry a potential risk of distortion of the imaging information. There was no clear consensus about MRI negative tumours and their clinical significance, although these will be formally identified as part of the evaluation and further defined with experience in the technique.

The use of scolopamine in MRI was not agreed amongst the radiological subsection of the meeting and this has been listed for further evaluation between the centres.

Surgical Practice

The consensus group agreed on the distribution of systematic cores in defined sectors: the peripheral zone (PZ) and the anterior zone should be biopsied preferentially (Fig. 1). Variations of numbers of biopsies should be considered depending on the size of the gland (Table 3).

Biopsies of anterior zone (= anterior sector divided into right and left) (pink).

In total, four or five biopsies from medial to lateral taken from the anterior apex of the prostate.

Biopsies of the apical PZ (= mid-sector divided into right and left) (green).

In total, four to six biopsies from medial to lateral taken from the apex of the prostate.

Table 2 Summary of definitions with agreement, including a minimum and optimal requirement.

Topic	Requirements	
	Minimal	Recommended (if applicable)
Definitions		
Zones	McNeal's zones [15]	
Surgical sectors	Division of the prostate into six to eight surgical regions to place biopsies and allow geographical separation	
Maps	No consensus reached	A geographical representation of the prostate to allow communication between specialties
Template biopsy	Replicated predefined core distribution pattern for transperineal prostate biopsies	Transperineal biopsies of the prostate according to a predefined systematic pattern (may differ dependent on whether primary or secondary biopsy)
Transperineal biopsy	Biopsies taken through the perineum with the patient in the lithotomy position under TRUS guidance	
Saturation biopsy	More than 20 biopsies of the prostate with the intention of comprehensively sampling the prostate, regardless of technique	
Extended transrectal biopsy protocol	More extensive number of biopsies taken transrectally involving peripheral and transition zones: biopsying defined sectors – sextant, anterior horn peripheral zone, transition zone and midline [15]	
Cognitive MRI-supported biopsy	Directed biopsies using MRI information and TRUS guidance but without fusion overlay (cognitive)	
MRI/TRUS fusion biopsy	Targeted biopsies with MRI information using MRI/TRUS fusion overlay technology	
Mapping biopsy	Exhaustive transperineal TRUS-guided biopsies using a 5-mm brachytherapy grid, with at least one biopsy from each hole, according to Barzell [15]	
PSA level rise	Two consecutive rises in PSA level above baseline	
Suspicious PSA velocity	PSA velocity, which is defined as an absolute annual increase in serum PSA level (ng/mL) >0.35 per year [15]	
Persistent suspicion	Histological, clinical or radiological suspicion of prostate cancer after previous negative prostate biopsy	
Normal PSA level	Locally agreed normal ranges (as per local laboratory)	
Clinical suspicion of malignancy	Suspicious rectal examination (DRE) and/or raised PSA level above age-related normal range	
Active surveillance	Continual monitoring in a population of patients with localized prostate cancer, with a view to curative intent, according to locally agreed pathways	
New presentations	Patient with suspicion of prostate cancer: abnormal PSA level, DRE or risk factors	
To be recorded dataset for previous biopsies	Record number of biopsy studies, time between biopsies and high-grade prostatic intraepithelial neoplasia/atypical small acinar proliferation if applicable	In addition, record the number of previous cores and protocol of biopsy (i.e. sextant, malondialdehyde or transperineal)
Active surveillance biopsy	A prostate biopsy as part of an active surveillance protocol.	As per minimal but biopsy taking place between 3 and 6 months from the commencement of active surveillance
Biopsies in previously treated patients	Patient's suspected as local failure after a primary treatment	
Restratification biopsy	Repeat biopsies to define disease when there is uncertainty about treatment modality	
Contraindications for TRUS-guided sector biopsy?	Local anatomical problems (e.g. absence of rectum/anus) or medically contraindicated (e.g. unfit for anaesthesia)	
Imaging		
Acquired MRI sequences	T1, high-resolution T2 and diffusion-weighted image (including apparent diffusion coefficient map calculation)	Dynamic contrast-enhanced, spectroscopy
Enema	Not routine	
Scopolamine	No consensus	
Positioning	Use of a crural wedge to tilt the pelvis	
Reporting proforma: focus	Primary reporting of target lesions	In addition to target lesions, primary reporting of all sectors to be biopsied
Reporting proforma: localization	Location recorded for each target using a standardized localization map in written report or drawing	
Reporting proforma: scoring	Subjective significance score given by radiologist (1, very low probability; 2, low probability; 3, equivoval; 4, high probability; 5, very high probability)	In addition, scoring in five grades of each modality (T2, diffusion-weighted image, perfusion imaging, etc.) separately (PI-RADS [prostate imaging, reporting and data system] based) [14]

Table 2 Continued.

Topic	Requirements	
	Minimal	Recommended (if applicable)
Surgical protocol with definitions		
Physical environment	Should be performed in theatres with resuscitation equipment readily available	
Manpower requirements	Surgeon, support staff, scrub nurse	
TRUS	Curvilinear/convex transducer in transverse and sagittal view; frequency 5–12 MHz; focal range 3–60 mm; frame rate/td >150	A linear transducer in sagittal view should be used
Preoperative preparation		
Anticoagulation	Aspirin can be continued but cumarin derivates (warfarin) and clopidogrel ideally must be stopped, unless medically contraindicated	
Enema/suppository	The use of a suppository is recommended ideally 1 h before the procedure to improve ultrasonographic visualization of the prostate	
Antibiotic policy	Dependent on antibiotic and infection history. Commonly: ciprofloxacin 500 mg orally 1 h before surgery and for 3 days after surgery	Evidence is to be built to support any antibiotic policy for transperineal biopsies. This is a required point of research
General anaesthetic	Preferred but other techniques may be employed	
Spinal anaesthetic	Can be used	
Local/regional anaesthetic	Item to be investigated (movement artefact may compromise accuracy in fusion techniques)	
Positioning		
Lithotomy	Lithotomy (extended, if required)	
Symmetry	The pelvis and legs must be symmetrical and the perineum in the midline of the table	
Scrotal support	'Heidelberg sling' (the patient's gown is brought down over the lifted scrotum and taped in place) or 'Chinese dressing of Guy's' (wide tape is placed from under the lifted scrotum to the sternum)	
TRUS placement and image set-up		
Probe angle	The aim is to avoid distortion. Although no angle can be prescribed, this real-time figure depends on pelvic position, pubic arch position and relation of axis of rectum and posterior prostate on MRI (for fusion purposes)	
Distance of rectal wall to prostate	This should be modelled on the MRI scan and the trace should be parallel to the posterior prostate	
Compression of prostate	Using a balloon condom, compression should be avoided if at all possible using a minimal volume of water in balloon	
Prostate symmetry	The prostate should be in the midline and symmetrical	
Battleship grids	5-mm battleship grids are the standard recommendation	2.5- or 5-mm grids should be used
Biopsy placement		
Core distribution first biopsy	It was agreed to adapt the sector approach developed at Guy's Hospital, London. The peripheral zone is the preferential target. This is to be used for all indications. Separate biopsies are to be taken from MRI-suspicious lesions. There was unanimous agreement that biopsies of target lesions alone are obsolete on the basis of the current imaging	
Core distribution for second or active surveillance biopsy		
Large prostate		
MRI lesions	Depending on the size of the lesion but, as a minimum, two cores should be taken from each target lesion	Depending on size, two to four cores should be taken from the lesion and two cores adjacent to the lesion
Needle deviation techniques	Although discussed, this is based on surgical preference and skill and no consensus is appropriate here	
Postoperative care		
Ciprofloxacin cover	It was agreed that, although there was no evidence for routine post-procedure antibiotics use in transperineal biopsies, the routine use of 3 days of postoperative ciprofloxacin is almost universal	Evidence is to be built to support any antibiotic policy for transperineal biopsies. This is a required point of research
Tamsulosin	With a clinical indication, tamsulosin may be considered, although it is not routinely recommdended.	
Catheter	The use of a catheter was not routinely recommended	
Complications		
Recording	All complications, including erectile dysfunction, acute retention of urine, haematuria with or without retention and infection (including urosepsis), should be documented	
Histology		
Specimen marking, quality control and preservation		

Table 2 Continued.

Topic	Requirements	
	Minimal	Recommended (if applicable)
Inking for localization or basal–apical orientation	Not routinely used	Inking with fixation of all cores used for localization/orientation for radiological feedback (precision learning process only, which may help to identify MRI invisible lesions)
Length measurement	There was unanimous opinion that the quality control standard for transrectal biopsies (17 mm) cannot be expected. The areas biopsied by transperineal approach have often a more loose consistency. The ideal minimum length of each core should be 10 mm	
Formalin fixation	Formalin fixation is routinely recommended	
Specimen processing		
Single/multiple cores	Maximum of five cores per block. The number of sections taken should ensure full-face assessment of the cores and availability for immunohistochemical investigation	
Reporting proforma		
Number of cores	To be recorded	
Length of cores	To be recorded (macroscopic)	
Modified Gleason score [14]	The most prevalent and worst Gleason scores should be recorded in a standard A plus B format (e.g. 3 + 4 = 7)	As minimal but should include percentage of Gleason 4 and 5 as a tertiary score
Core localization	Localization of cores within the sectors or targets should be facilitated down to an accuracy of four cores because bringing it down to one core would be a significant increase in workload for some centres	Report each core in relation to individual localization and orientation in the prostate (if supported by inking and single core processing)
Proportion of cancer involvement	There is no internationally agreed standard of reporting; tumour density, length (mm) and percentage of involvement of core or specimen were considered. Centres are asked to provide at least one of the above in conjunction with the overall number of cores in the specimen and length of all cores to allow subsequent mathematical extrapolation to any parameter required for meaningful scientific analysis	Both lengths and percentage reported
Atypical small acinar proliferation	Accepted as per international definitions	
High-grade prostatic intraepithelial neoplasia	As per international definitions and recorded unifocal and multifocal (more than one core) prostatic intraepithelial neoplasia	
Inflammation	Granulomatous prostatitis and significant prostatitis should be reported	Ideally, all significant inflammation will be recorded

Biopsies of the posterior PZ (= posterior sector divided into right and left) (red).

In total, four to six biopsies from medial to lateral taken from the apical end of the prostate.

The additional requirements for prostates more than 4 cm long are outlined below.

Biopsies of the basal PZ and posterior transition zone (basal sector divided into right and left) (orange).

In total, four to six biopsies from medial to lateral taken from the basal half of the prostate after placing the biopsy needle through the apical half of the prostate.

Lesions

In total, two to four biopsies should be taken from each targeted lesion before systematic biopsies.

There were two areas that were highlighted in the surgical practice discussion. These were the antibiotic protocol and the use of tamsulosin after surgery. There is little literature available on the appropriate use of antibiotics and the anecdotal incidence of postoperative sepsis is reported to be extremely low after transperineal biopsy. There was agreement across the group that there was a need to work towards defining the place or requirement for antibiotics in patients undergoing transperineal biopsies. Consensus was reached that peri-operative catheterization is not required because acute retention rates are low for sector biopsies [16]. Accordingly, the routine use of tamsulosin was not recommended unless there was considered to be a significant risk of retention in patients with large prostates or moderate to severe LUTS. Retention rates should be a focus for collaborative studies because the overall rates of postoperative acute urinary retention are low and multicentre data collection will allow this question to be addressed more efficiently.

The meeting agreed on the minimal requirements for the TRUS probe used. The specifications are listed in Table 2.

Pathology Analysis

There was considerable uncertainty during the discussions about histological analysis and reporting. The panel of pathologists unanimously agreed that the analysis of specimens and reporting standards must be deliverable by

Fig. 1 Preferable distribution of systematic cores.

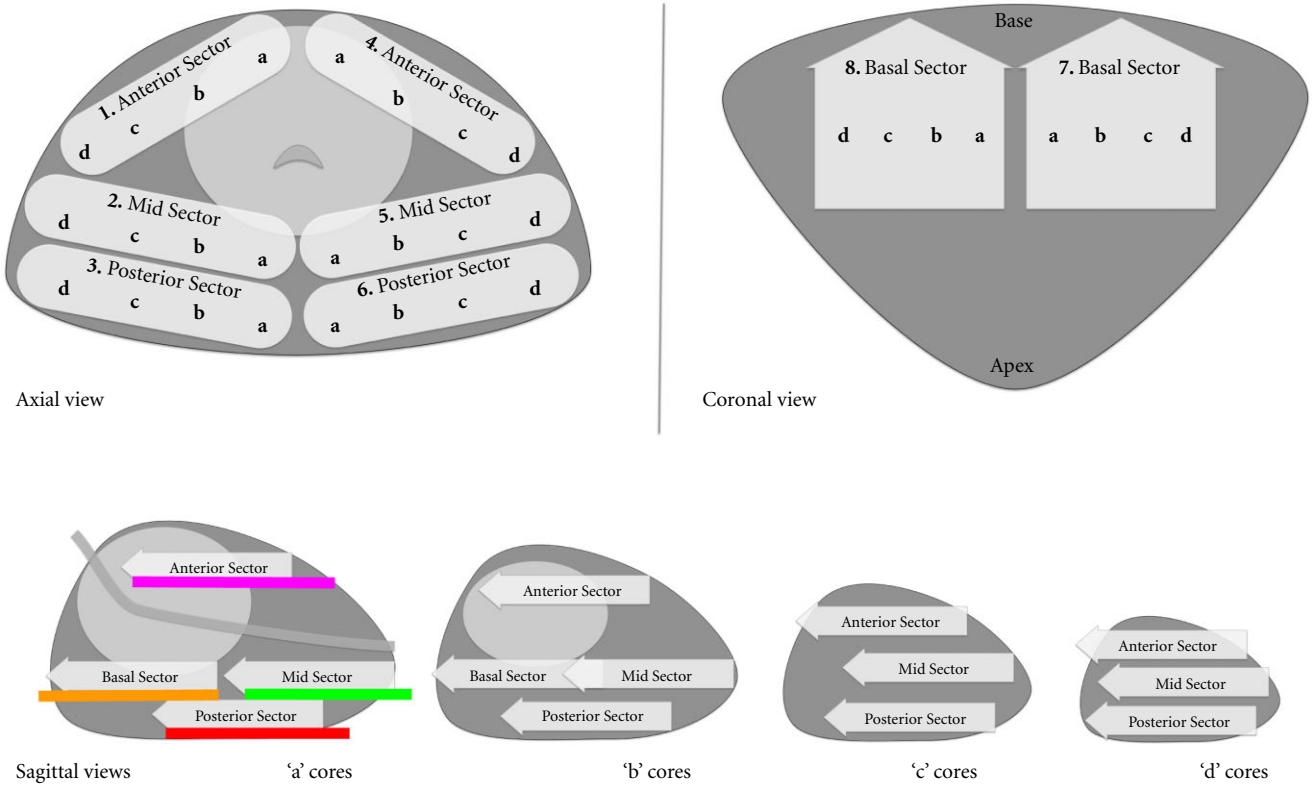

Table 3 Variation of the number of biopsies depending on the size of the prostate: transperineal 'sector' biopsy protocol.

Prostate volume (mL)	Number of cores taken per sector (right + left)				Total number of cores
	Anterior	Mid	Posterior	Basal	
0–30	4 + 4	4 + 4	4 + 4	0	24
>30–50 and length >4 cm	4 + 4	4 + 4	4 + 4	4 + 4	32
>50 and length >4 cm	5 + 5	5 + 5	5 + 5	4 + 4	38

the existing workforce and within routine laboratory and technical capacity. This was accepted by the whole group at the meeting. Some pathology departments were able to report on each single core with full localization across a sector describing the apical to basal distribution of cancer. Some preferred grouping specimens only by sector involvement. The minimum requirement was that the sector involvement and numbers of cores involved per sectors should be reported. Biopsies of lesions should be sent and reported separately from their sector.

The reporting of tumour volume per specimen differed significantly from cancer network to cancer network. For example, some centres reported a positive specimen by percentage involvement of cancer within a core; some by a percentage of the tissue involved from a given container; and some by percentage of the tissue submitted for one laterality. The consensus group considered it important that each centre is able to work within their existing framework but still provide a fertile ground for collaborative research to be nurtured. The final agreement on chosen parameters to be reported should allow mathematical extrapolation from one reporting method to another. In addition to the percentage of specimen involvement, the number of overall cores, mean length and range of length are to be recorded in the database. The inking of cores to identify their apico–basal orientation was regarded as the ideal standard to provide the most accurate feedback for MRI image interpretation and to improve MRI reporting by correlation of histopathology with MRI images and also the facilitation of focal therapies.

Minimum Dataset

The Ginsburg study group agreed on a minimum dataset, as outlined below.

Patient data

Name, date of birth, age.

Previous Biopsy (for each previous biopsy separately)

Date of biopsy, finding of rectal examination (DRE), PSA level, number of cores, prostate volume, histological finding (prostatic neoplasm, significant atypical changes and high-grade prostatic intraepithelial neoplasia), grading of PCa: Gleason score A and B and Gleason sum.

Indication for transperineal prostate (TP) biopsy

Raised PSA level, abnormal DRE, etc.

MRI (for each lesion separately)

Date of MRI, region of lesion, PI-RADS (prostate imaging, reporting and data system) score, significance score, TNM stage, name of radiologist.

TP biopsy

Date of biopsy, PSA level, number of cores, prostate volume, mean and range length of core.

TP biopsy histology

Sector of origin, number of cores per sector, positive cores per sector and targeted biopsy, histology of PCa: Modified Gleason score (most predominant and worst Gleason grade) [17,18] and a comparable quantitative measure of tumour extent [19].

Summary

Benign, PCa, atypical changes, etc.

Complications

None, acute retention, etc.

A corresponding data sheet is available on request from the corresponding author.

Discussion

There was a significant trend towards consensus in most areas, as well as with respect to minimum standard operating procedures. Patient populations, definitions of PSA dynamics, differing biopsy techniques/technologies and preferential anatomical components of the prostate were clarified. There are significant implications resulting from this process with respect to both clinical and research settings. This is the first group of its kind to attempt to bring together opinion on transperineal biopsies and, particularly, to incorporate technological advances such as MRI fusion. It has created an exciting clinical tool because diagnostic uncertainty remains as a significant issue in PCa management.

Multiparametric MRI techniques, protocols and the technology for biopsy using MRI/TRUS fusion technology are still emerging. As this technology develops and evolves, there will be a need for regular revision of the terms and protocols involved to keep up with the rapid changes occurring in a developing field. Although the current definitions and protocol are based on the latest evidence available, this will not necessarily be the case in the future.

The methodological limitations of our approach centre on the expert group discussion. In these settings, there is inevitable bias involved, where certain personalities may dominate and their opinions influence the outcome. Significant work was carried out aiming to eliminate such bias and to ensure that all discussion was based on pre-determined points and led by impartial chairs (Boris Hadaschik and Christof Kastner) who were rotated. The list of items for discussion was circulated in advance to all of the centres to ensure that the opinions and definitions from each centre (including their protocols) were included in advance of the face-to-face meeting. The list was collated in advance and formed the basis for discussion so that all centres were equally represented. Where possible, the most recent peer-reviewed evidence on a given topic or item for discussion was distributed in advance and used during the discussion and, where possible, referenced within the document. The chair ensured that members from each centre were happy with the decision of the group and a 'show of hands' voting system was employed amongst all of those present.

The other major limitation with any consensus group is that, although the work described in present study represents the views and opinions of our centres, who are united by a common interest with respect to the preferential targeting of the PZ and anterior zone and have experience of using MRI in their biopsy process, it does not include the views of all those who currently perform transperineal biopsies in our respective countries, the rest of Europe or the USA. This limits the outcomes to a statement of our current practice rather than a formal consensus document on transperineal biopsies as a whole. It is our hope that, with increasing interest in targeted biopsies of MRI visible lesions and selected sampling of the PZ and anterior zone, there will be the opportunity to involve other centres within our consensus group as associates. We intend to hold regular meetings allowing us to evaluate and incorporate the latest literature and coordinate the opportunity for collaborative research and publication.

Surgical technique was honed and outlined, allowing good recommendations to be defined with significant consensus. Importantly, as well as technical issues, standard biopsy protocols and sampling patterns were agreed amongst members. Before the meeting, each collaborating centre had

separately established own techniques. Using the evidence available in the literature [5–8,16], as well as considering factors relating to funding, biopsy techniques had been favoured that allowed the limitation of cores by systematic core distribution. At the very minimum, each centre had audited and published the outcomes of their technique as posters and papers [16], which supported the decision-making process with respect to finding a common standard. Of the four centres, two had attempted and audited the Barzell mapping approach [15], reaching the conclusion that increased side-effects and the impact on pathology departments would not justify such an approach.

To ensure widely acceptable consensus on this field, the available literature [5–8,16] was discussed. Although the literature highlights the high value of biopsies from the PZ, additional biopsies from the TZ were included as a result of clinical experience. The distribution of the biopsies was described for different areas of the prostate using the terminology of 'sectors' (as proposed by the team of Richard Popert from Guy's Hospital London). This is a unique achievement in an area where there has been no clarity in the past. We acknowledge that, until now, there has been no evidence on the usefulness of 'sector' distribution and further descriptions and outcomes aiming to validate this approach are being developed. Further work will aim to define predetermined computer-generated biopsy patterns based on histological cancer detection rates and tumour volume definitions that are considered clinically important. As noted above, differing histological reporting analysis was one of the most contentious issues. Further work will be necessary to ensure that we can define and apply the minimum dataset and reporting proforma to take into account differing local technical considerations.

Subsequent to the advent of testing PSA levels, the detection of PCa has relied on biopsies alone. Imaging modalities have improved significantly and it is possible that, in the future, technologies such as MRI fusion targeting of radiologically defined lesions may be sampled with sufficient accuracy so that random biopsies become unnecessary. If MRI becomes sufficiently accurate to identify biologically significant disease and exclude insignificant disease, then biopsies of anything other than the identified lesion may not be required, particularly with negative MRIs. However, this remains conjecture and, although attractive in concept, the only way to prove the value of MRI in this setting will be to accurately record and systematically document the diagnostic accuracy and, particularly, negative-predictive value of MRI within a multicentre setting. Ideally, this should comprise a multicentre, randomized study with long-term follow-up. Only in this way would it be possible to feedback and, using a multidisciplinary approach, improve the reliability of surgical and radiological techniques.

The ultimate goal is to improve patient care by minimizing harm and optimizing the diagnostic pathway. Transperineal biopsies have been shown to reduce the random and systematic error within transrectal biopsies, and so they are more accurate in a research setting [14]. Further work should combine transperineal biopsy and MRI in a prospective randomized trial to define best practice and diagnostic accuracy compared to cognitive directed and mapping techniques.

In conclusion, the Ginsburg study group agreed on definitions of common terms and practice related to transperineal prostate biopsy procedures and has created a minimum dataset to facilitate a joint database between the collaborative centres and other associated centres that are willing to join the group. The creation of this collaborative database comprises the essential component for enabling multicentre evaluation and studies in this field of research. The ability to detect, locate and characterize PCa both radiologically and pathologically with a high precision has significant implications for the diagnostic pathway. Our hope is that this approach will reduce the impact of the assessment on the patient and be more cost effective on the healthcare system, as well as ultimately reduce uncertainty for patients.

Our intention is not to be prescriptive on how transperineal biopsies should be carried out but, instead, to stimulate others to contribute to discussions on technique, as well as engage in our efforts that aim to improve and develop the technique. It is key that research is prioritised to areas with little or no consensus and that they must be embedded within prospective trials and cohort studies. The key areas that need to be supported by evidence are the indications for transperineal biopsies, primary and secondary diagnostics, risk stratification in active surveillance, the value of pre-biopsy MRI or other similar imaging, and the role of cognitive MRI supported biopsies and MRI-ultrasonographic fusion. The use of peri- and postoperative antibiotics and α-blockers needs to be explored. Finally, a long-term assessment needs to be undertaken to assess the reassurance that negative or normal transperineal prostate biopsies provide to patients, particularly the avoidance of repeated biopsy because their risk of PCa is low. Again, as in most matters concerning PSA levels, the resolution of uncertainty with well designed and appropriately powered multicentre studies is paramount for addressing the health economic implications of this approach as an alternative to transrectal biopsies.

Acknowledgements

We thank Medcom for their support in financing the first meeting of our study group.

Conflict of Interest

None declared.

References

1 **Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D.** Global cancer statistics. *CA Cancer J Clin* 2011; 61: 69–90

2 **Schröder FH, Hugosson J, Roobol MJ et al.** Prostate-cancer mortality at 11 years of follow-up. *N Engl J Med* 2012; 15: 981–90

3 **Moore CM, Robertson NL, Arsanious N et al.** Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. *Eur Urol* 2013; 63: 125–40

4 **Batura D, Rao GG, Nielsen PB.** Prevalence of antimicrobial resistance in intestinal flora of patients undergoing prostatic biopsy: implications for prophylaxis and treatment of infections after biopsy. *BJU Int* 2010; 106: 1017–20

5 **Onik G, Barzell W.** Transperineal 3D mapping biopsy of the prostate: an essential tool in selecting patients for focal prostate cancer therapy. *Urol Oncol* 2008; 26: 506–10

6 **Ayres BE, Montgomery BSI, Barber NJ et al.** The role of transperineal template prostate biopsies in restaging men with prostate cancer managed by active surveillance. *BJU Int* 2012; 109: 1170–6

7 **Bott SRJ, Henderson A, Halls JE et al.** Extensive transperineal template biopsies of prostate: modified technique and results. *Urology* 2006; 68: 1037–41

8 **Chun FK-H, Epstein JI, Ficarra V et al.** Optimizing performance and interpretation of prostate biopsy: a critical analysis of the literature. *Eur Urol* 2010; 58: 851–64

9 **Fink A, Kosecoff J, Chassin M, Brook RH.** Consensus methods: characteristics and guidelines for use. *Am J Public Health* 1984; 74: 979–83

10 **Pill J.** The Delphi method: substance, context, a critique and an annotated bibliography. *Socio-Econ Plan Sci* 1971; 5: 57–71

11 **Leape LL, Hilborne LH, Schwartz JS et al.** The appropriateness of coronary artery bypass graft surgery in academic medical centers. Working Group of the Appropriateness Project of the Academic Medical Center Consortium. *Ann Intern Med* 1996; 125: 8–18

12 **Tobacman JK, Lee P, Zimmerman B, Kolder H, Hilborne L, Brook R.** Assessment of appropriateness of cataract surgery at ten academic medical centers in 1990. *Ophthalmology* 1996; 103: 207–15

13 **Hunter DJ, McKee CM, Sanderson CF, Black NA.** Appropriate indications for prostatectomy in the UK – results of a consensus panel. *J Epidemiol Community Health* 1994; 48: 58–64

14 **Dickinson L, Ahmed HU, Allen C et al.** Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. *Eur Urol* 2011; 59: 477–94

15 **Barzell WE, Melamed MR.** Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3-dimensional pathologic mapping of the prostate – a 4-year experience. *Urology* 2007; 70 (Suppl.): 27–35

16 **Hadaschik BA, Kuru TH, Tulea C et al.** A novel stereotactic prostate biopsy system integrating pre-interventional magnetic resonance imaging and live ultrasound fusion. *J Urol* 2011; 186: 2214–20

17 **Egevad L, Mazzucchelli R, Montironi R.** Implications of the International Society of Urological Pathology modified Gleason grading system. *Arch Pathol Lab Med* 2012; 136: 426–34

18 **Epstein JI, Allsbrook WC, Amin MB, Egevad LL, ISUP Grading Committee.** The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol* 2005; 29: 1228–42

19 **Fine SW, Amin MB, Berney DM et al.** A contemporary update on pathology reporting for prostate cancer: biopsy and radical prostatectomy specimens. *Eur Urol* 2012; 62: 20–39

Correspondence: Dr Boris Hadaschik, Department of Urology, University Hospital Heidelberg, Heidelberg, Germany.

e-mail: hadaschik@gmail.com

Abbreviations: PCa, prostate cancer; PZ, peripheral zone; RAM, Research and Development/University of California Los Angeles Appropriateness Method; TP, transperineal prostate.