Refining Partial Gland Ablation for Localized Prostate Cancer: The FALCON Project

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Conflict of interest statement

The authors disclose the following potential conflicts of interest:

Lara Rodriguez-Sanchez is involved in consulting and speaking engagements for AngioDynamics. Additionally, she received speaker fees from EDAP-TMS. **Phillip Stricker** serves as a consultant for AngioDynamics. **Mark Emberton** receives research support from the United Kingdom National Institute of Heath Research (NIHR) via the UCLH/UCL Biomedical

Research Centre. He acts as a consultant/lecturer/proctor for Sonacare Inc; Angiodynamics Inc; Early Health and Albermale Medical. **Bernardino Miñana Lopez** declares consulting fees from Janssen, Astellas, AstraZeneca, Sanofi, Merck, Amgen, Bayer, Werfen, and AngioDynamics. Additionally, he discloses being a proctor for Irreversible Electroporation (Nanoknife), HolEP, and prostate robotic surgery, and receives compensation for training other surgeons in these procedures. **Jose Luis Dominguez-Escrig** declares participation in Clinical Trials from IPSEN Pharma, Janssen, Arquer Diagnostics, Combat BRS, Presurgy, Physion, STORZ and Angiodynamics. Additionally, he declares consulting fees from Angiodynamics and he is currently proctor for Irreversible Electroporation (NanoKnife). **Fernando Bianco** serves as a scientific advisor for Angiodynamics. Additionally, he is an investigator for Clinical Laserthermia Systems, SE, and ELESTA SPA, but has never received compensation directly or indirectly from these companies. Furthermore, he is an investigator for Janssen Pharmaceuticals and Merck but has not received any payment from them or from any company that he owns. He also holds a shareholder and leadership position in Focalyx. **Georg Salomon** declares that he has received honoraria, specifically lecture fees, from EDAP**, Alberto Bossi** has received grants and research support from Janssen, Ipsen, and Sanofi, and has also received honoraria from Accord, Astellas, Elekta Brachytherapy, Ipsen, and Recordati. He participates in advisory boards for Accord, Astellas, and Elekta Brachytherapy. **Robert Reiter** is engaged in consulting and speaking arrangements with Janssen, Lantheus, Bayer, Pfizer, and Astellas. **Luca Lunelli** provides consulting and speaking services for AngioDynamics. **George R Schade** serves as a consultant for EDAP Technomed, Inc. Additionally, he acts as an advisor for Immunity Bio. He also has intellectual property licensed to Petal Surgical. Furthermore, he declares research funding, which includes grants from the National Institutes of Health (NIH) under grant numbers R01DK119310 and R01CA258581, as well as support from the American Cancer Society under grant number RSG2117101. **Veeru Kasivisvanathan** received speaker fees for lectures on prostate cancer from the European Association of Urology, Singapore Urology Association, and Clinical Comms Group. **Thomas J Polascik** is involved in studies supported by Janssen Bladder Cancer, Myovant Sciences, Prostatype Genomics, Merck, Astellas mCSPC and Astellas mHSPC. **Ardeshir R Rastinehad** declares consultant and research support for Philips Healthcare. Rafael Sanchez-Salas declares serving as a Speaker and Consultant for Abbvie Canada, EDAP-TMS, ExactImaging, and Angiodynamics, with the Angiodynamics involvement also noting a spousal relationship.

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Abstract

Objectives: To provide a contemporary statement on focal therapy (FT) for localized prostate cancer (PCa) from an international and diverse group of physicians treating localized PCa. This effort aims to overcome the limitations of previous consensus statements, which were restricted to early adopters, and to offer direction on the various aspects of FT application that are currently not well-defined.

Materials and Methods: FALCON started as a 154-item online survey developed following a steering committee discussion and literature search. Invitations to participate were extended to a large, diverse group of professionals experienced in PCa management. From 2022 to 2023, three rounds of Delphi consensus using the Modified Delphi method were performed with a 1-9 Likert scale followed by an in-person expert meeting. The threshold for achieving consensus was set at 70% agreement/disagreement. Six main areas of FT were covered: 1) patient selection, 2) energy source selection, 3) treatment approach, 4) treatment evaluation and follow-up, 5) treatment cost and accessibility, and 6) future perspectives.

Results: Out of 246 initial participants, 148 (60%) completed all three rounds. Based on participant feedback, 27 new statements were added in the second round, and 33 questions related to personal expertise for which consensus was not necessary were excluded. After the third and final round, 69 items did not reach consensus. These items were discussed at the in-person meeting resulting in a consensus of 57 additional items. Consensus was finally not reached on 12 items. Given the volume of data, the voting outcomes are summarized in this article, with a detailed breakdown presented in the form of figures and tables.

Conclusions: The FALCON project delivered a significant consensus on the approach to FT for localised PCa. Additionally, it highlighted gaps in our knowledge that may provide guidance for future research.

Keywords: prostate cancer, ablation techniques, Delphi study, consensus, patient selection, energy source selection, treatment evaluation

Introduction

Worldwide in 2020, over 1.4 million men were diagnosed with prostate cancer (PCa) [1], with approximately 80% at local or regional stage. The large number of affected men combined with the adverse effects of standard treatments like radical prostatectomy and radiation therapy on sexual, urinary, and bowel function [2], makes exploring alternative treatments imperative.

In response to this issue, initially active surveillance emerged as a means of delaying or avoiding treatment. However, it is important to note that this approach is not recommended for all patients.[3] Focal therapy (FT) was developed to address this gap with the objective of improving functional outcomes for men with localised PCa who are not eligible for active surveillance without compromising oncological outcomes. Nevertheless, currently, data supports the functional benefits of FT including minimal impact on continence and erectile function [4], but evidence from long-term oncological outcomes from clinical trials and well-designed registries remains scarce.

FT evolved hand in hand with technology. Nowadays, the cornerstone of FT is the deployment of magnetic resonance imaging (MRI) to precisely identify the location of the index lesion and to guide target biopsies and treatment to the lesion considered to drive PCa towards a lethal metastatic state [5, 6]. In the future, lesion localization and staging might be further refined with novel technologies such as micro ultrasound, prostate-specific membrane antigen positron emission Tomography (PSMA PET), epigenetics, and artificial intelligence which may refine MRI interpretation and further advancements in the field [7–9]. Regarding treatment planning, lesion targeting can be achieved via cognitive or software-based fusion, with the choice of energy source and application route (transperineal, transrectal, transurethral) depending on lesion characteristics [10, 11].

Heterogeneity in the field of FT stemming from this rapid evolution of technologies presents a challenge as it leads to changes in medical practice before outcomes have been thoroughly evaluated. Variations in patient selection, treatment, and follow-up protocols impede the evaluation of comparative oncologic outcomes. Furthermore, guidance is limited on controversial issues in the field of FT including debate over patient selection, type of energy to be used, and timing and method of post-treatment biopsies [12]. Uncertainty on such topics underscores the need for an updated consensus while in parallel more robust studies addressing these issues are conducted.

Prior FT consensuses were developed to address the aforementioned issues. Still, they faced several limitations, such as only including pioneers and early adopters of FT, which may provide a biased viewpoint. Furthermore, most focused solely on patient selection, treatment, or follow-up rather than addressing a broader range of debated topics about FT. While these studies were published, results were not necessarily considered in real-world clinical practice. A large and diverse pool of participants is needed to improve the quality of consensus and promote the application of its results [12]. For these reasons, the FocAL therapy CONsensus (FALCON) project was created to address the controversial aspects of FT by establishing a broad, international consensus from a large number of physicians with diverse backgrounds with the ultimate with the goal of having an impact on real-world practice.

Materials and Methods

Literature Review

A 154-item English questionnaire was developed after a steering committee meeting followed by a non-systematic literature review to determine gaps in FT knowledge. The steering committee members are detailed in the Supplementary Appendix. In November 2022, The PubMed database was searched for articles published in English from October 2012 to October 2022 using the terms "focal therapy" AND "prostatic neoplasms" with a focus on identifying systematic reviews and previously published Delphi consensuses. Based on this information a survey was designed and divided into six sections: 1) patient selection, 2) energy source selection, 3) treatment approach, 4) treatment evaluation and follow-up, 5) treatment cost and accessibility, and 6) future perspectives.

Participants

Stakeholders specialized in different domains of PCa care were invited to participate in the Delphi consensus. Specialties included urologists, medical oncologists, radiologists, radiation oncologists, and pathologists. Participants were recruited via direct mail from steering committee members, with support from the Focal Therapy Society (FTS), the Confederación Americana de Urología (CAU), and the Société Internationale d'Urologie (SIU), who promoted the project on social media. To maintain control, direct access to the survey through social media was not allowed.

Consensus Development

The FALCON project used the modified Delphi method [13, 14]. Given the lack of consistency in the Delphi methodology, with slight variabilities among different studies, a protocol was developed to predefine the survey design. This included the sections and statements to be included, the stakeholders involved, strategies for distributing the survey, and the threshold for consensus [15–17]. From December 2022 to October 2023, three rounds of Delphi consensus were conducted using the web-based DelphiManager software (Liverpool, UK) [17]. The survey used a 1-9 Likert scale (1–3 disagree; 4–6 equivocal; 7–9 agree) with an option for "Unable to rate". At each subsequent round, the results of the prior round were shared, and participants were reminded of their responses. Participants were allowed to change their responses, share feedback on the statements, and suggest new statements to improve the survey for the next round. The threshold for consensus was set at a minimum of 70% (agreement or disagreement) of the respondents. After the second round, which included all statements from the first round plus those added by the respondents, all statements that reached consensus and those related to personal expertise for which consensus was deemed unnecessary were removed. For the project`s final phase, a 4-hour in-person meeting was held on October 12th, 2023, in Istanbul, Turkey, and included in-person and virtual attendees. This phase included a fourth survey followed by a discussion to attempt to achieve consensus on items that did not reach consensus in prior rounds. Items that reached consensus previously were also discussed, and if needed, were modified slightly to improve clarity for future readers.

Results

Literature Review and Survey Development

Results from the literature review yielded 14 systematic reviews and 9 Delphi consensuses on FT (Supplementary Tables 1 and 2). Based on the results of this search, the survey was divided into the six sections as described above. These domains were further divided into the sub-domains depicted in Figure 1.

Participant Information

Out of 246 initial participants, 148 (60%) participated in all three Delphi rounds. Most participants in each of the three rounds were urologists though radiation oncologists, radiologists, pathologists, and oncologists were also represented (Figure 2).

Survey Results

A flowchart of the Delphi process is included in Supplementary Figure 1. Briefly, the survey started with 154 items. Twenty-seven new statements were added in the second round based on respondent suggestions. Thirty-three statements related to personal expertise were excluded after the second round. Results from these statements are presented in Supplementary Table 3. Statements reaching consensus during the second and third rounds were removed from subsequent rounds. Statements that reached consensus after the three online rounds are presented in Supplementary Tables 4 with 53 statements reaching consensus in round 2 and 25 in round 3.

After the third and final online round, 69 statements did not reach a consensus. These statements were included in a fourth survey completed by attendees at the beginning of the in-person meeting. Through this survey, an additional 50 statements reached consensus and were subsequently discussed to validate the results (Supplementary Tables 5 and 6). During the in-person meeting, nine people participated in person, and five others connected via Zoom for at least one hour. Following an in-person discussion of the 19 statements that did not reach consensus in the fourth survey, seven additional statements reached consensus. In total, 135 items reached consensus after the three Delphi rounds and the in-person meeting.

All the statements that reached consensus are listed in Supplementary Table 7:

Patient Selection: Life Expectancy

The consensus was that age should not be a determining factor for FT; instead, life expectancy should be considered, and treatment should be avoided for patients with a life expectancy of less than 10 years.

<u>Patient Selection: Sexual Activity and Voiding Symptoms</u>

The ideal candidate for FT would be a sexually active man with mild to moderate voiding issues (whether treated medically or surgically) who seeks to treat his PCa with minimal impact on functional outcomes. However, this would not exclude men with erectile dysfunction or significant voiding symptoms from being suitable candidates for FT.

Patient Selection: Biopsies

According to the consensus, systematic bilateral biopsies combined with targeted biopsies are required prior to FT. Candidates should undergo 3-4 targeted biopsies (MRI in-bore biopsies, MRI/US fusion biopsies, or cognitive fusion biopsies) and 10-12 systematic biopsies, with saturation biopsies or transperineal mapping biopsies, as described by Winston Barzell, considered unnecessary.

It was agreed that FT should not be offered if MRI is unavailable, of low quality, or if MRI is negative while biopsies are positive. Moreover, there was consensus against the statement: "FT may be offered even if MRI is unavailable or of low quality, as long as mapping biopsies, as described by Winston Barzell, are performed." However, no consensus was reached regarding the statement: "FT should not be offered in cases of negative MRI and positive biopsies, even if mapping biopsies by Winston Barzell are performed" (statement 25, Table 1).

The presence of positive biopsies outside the MRI-detected lesion would not be an absolute contraindication for FT. FT may still be considered if unexpected out-of-lesion International Society of Urological Pathology (ISUP) 1 biopsies are found, regardless of their number, location, or proximity to the target lesion. Unexpected out-of-lesion ISUP 2 biopsies may also be acceptable, provided they are close to the target lesion and can be treated simultaneously.

Patient Selection: Number of Lesions on MRI

Multifocality on MRI would not contraindicate FT, with treatment reserved for lesions confirmed by anatomopathological findings from biopsies.

Patient Selection: Location of the Target Lesions

PSMA PET would not be considered a suitable replacement for MRI in selecting patients for FT. Lesions less than 5 mm from the rectum may be treated with FT, while lesions less than 5 mm from the sphincter should not be treated. However, maintaining a minimum 10 mm distance from the sphincter was not considered mandatory.

All lesions can be treated with FT, provided they can be safely accessed by the chosen energy source. During the final meeting, High-Intensity Focused Ultrasound (HIFU)and Irreversible Electroporation (IRE) were considered safe energy options for lesions close to the rectum, while IRE was deemed a safe energy source for lesions near the sphincter. No single energy source was considered to guarantee favorable oncological and functional outcomes for all lesion locations.

Patient Selection: Prostate Volume

According to the consensus, prostate volume is not a limiting factor if the lesion can be safely accessed. The prostate volume threshold varies by energy source and lesion location.

Patient Selection: Tumor Volume

Tumor volume on MRI was considered an important factor when treating PCa patients with FT. Tumor volumes greater than 1.5 cm^3 could be treated, and tumor volume ≤50% of the total prostate volume was also deemed suitable for FT. No statements regarding the treatment of larger tumor volumes were included in the consensus.

Patient Selection: PSA Level

PSA should be considered an inclusion or exclusion criteria for FT. Candidates may have a PSA value greater than 15 ng/ml, but PSA density should remain below 0.2, as determined during the final face-to-face meeting.

Patient Selection: Local Clinical Stage on MRI

Based on respondent opinions, local staging should be based on MRI rather than rectal examination. There was consensus that FT should not be offered if there is a likelihood of extracapsular extension (ECE) on MRI. While consensus was reached that patients with a clinical stage of ≤T2b on MRI are suitable for treatment, no consensus was reached on setting the threshold at ≤T2c for MRI-detected disease (statement 77, Table 1).

Patient Selection: Gleason Score

Over 70% of respondents agreed that FT should not be offered to patients with localized ISUP 1 PCa if they are eligible for active surveillance, but it may be offered to patients with ISUP 2 disease, regardless of the percentage of grade 4. Based on the final meeting, FT should be offered to patients with ISUP 3 PCa, but not to those with localized PCa greater than ISUP 3.

Patient Selection: Cribriform and Intraductal Patterns

There was consensus that FT may be considered over active surveillance for patients with localized ISUP 2 PCa (with a percentage of pattern 4 less than 10%) if a cribriform pattern is present. It was also agreed that patients with BRCA gene mutation should not be offered FT, and that the results of tissue genomic tests from biopsies (e.g., Decipher, Prolaris) could influence the decision to offer FT. On the other hand, participants agreed that germline genetic testing and tissue genomic tests from biopsies (e.g., Decipher, Prolaris) should be offered to all patients prior to FT.

Energy Selection

Regarding energy selection, the survey indicated that it should primarily be based on the surgeon's experience, with the preferred energy being the one the practitioner feels most confident using, as well as the location of the tumor. After the final meeting, it was agreed that HIFU or cryotherapy should be the first energy sources considered, as they are supported by the most data, even though much of it is retrospective.

Treatment Approach

Only the lesion identified on MRI, along with an appropriate safety margin, should be treated. Different energy modalities should be employed depending on the location of the index lesion. The minimal margin for treating the lesion was agreed to be 5 mm, with consensus against using 10 mm as the minimum margin. Additionally, there was consensus against considering hemiablation as the minimal treatment extension.

Treatment Evaluation and Follow-up

Based on the survey, patients should be followed for up to 10 years, with PSA testing every 3 months during the first year and then every 6 months thereafter. Early MRI, within a week after treatment, was not highly recommended, and based on the final face-to-face meeting, it should be performed on an annual basis. Regarding biopsies, 10-12 systematic plus 3-4 targeted biopsies should be performed at 12 months post-treatment, and then only if there is clinical suspicion. However, no consensus was reached on the possibility of follow-up using only PSA and MRI (statement 129, Table 1).

Functional outcomes should be assessed every 3 months for the first year, then annually until stability is achieved. The definition of PSA failure should depend on the ablation template used (lesion-only, quadriablation, or hemiablation), with consensus agreeing on the absence of a specific PSA failure definition after FT. Dedicated scoring systems for prostate MRI reporting post-FT should be developed and validated in a multicenter setting. Lastly, patients may be offered additional salvage FT following the failure of an initial treatment.

Future Perspectives

Respondents agreed on the importance of PSMA PET and the combination of systemic treatments and radiotherapy with FT in the future management of PCa treated with FT.

The 12 statements for which no consensus was reached are summarized in Table 1. These were primarily related to patient selection and follow-up. Specifically, there was no agreement on

whether to use transperineal or transrectal biopsy approaches when planning FT. Uncertainty also persisted about whether MRI-guided biopsies could be replaced by PSMA-guided or saturation biopsies prior to FT. Additionally, no consensus was reached on clinical staging or PSA thresholds, nor on the significance of intraductal and/or cribriform patterns. In terms of follow-up, disagreement remained regarding the definition of PSA failure, follow-up strategies with or without control biopsies using only MRI and PSA, and the role of PSMA PET in this setting. Treatment extent also proved controversial, particularly regarding the minimum necessary extension. Looking ahead, respondents were divided on the future role of FT in localized advanced PCa and oligometastatic scenarios.

Discussion

The FALCON project aimed to enhance the current body of literature by recruiting a large and diverse group of participants across multiple countries to address controversial aspects of FT. During the 10-year time frame of the literature review, at least nine consensuses on FT were published. Nonetheless, these studies focused on specific aspects of FT rather than taking a comprehensive approach. Additionally, the FALCON project with 148 participants completing the 3 Delphi rounds, overcame the limitation of past consensuses that rarely reached more than 50 participants for the third Delphi round [18–23].

While acknowledging that Delphi techniques are among the lowest levels of evidence for causal inference, it is still a useful methodology in cases–where gaps in the literature exist [13]. The FALCON project was developed to establish a contemporary and international consensus on how managing patients treated with FT from patient selection to follow-up. The goal was to include a wide and varied list of participants with different views on the same topics to reduce biases that may occur by including only one specialty of physicians or limiting participants to experts in the field.

Some relevant findings are particularly noteworthy and deserve to be highlighted. Regarding patient selection, inclusion criteria for FT are not standardized with variations in the threshold for PSA level, clinical stage, ISUP grade, number of lesions visible on MRI, and volume and location

of index lesion among others. One of the more controversial aspects of patient selection pertains to ISUP grade. As technology and experience evolve, leading to improved diagnostic and treatment accuracy, more aggressive forms of the disease are increasingly being treated [24]. While ISUP 2 is accepted as the best candidate for FT, there is debate over using FT for ISUP 3 PCa [23]. The FALCON project determined that FT should be offered to patients with localised ISUP 3 PCa and should not be offered to patients with localised >ISUP 3 PCa. Nevertheless, it should be acknowledged that although consensus on the role of FT for ISUP grade 3 and higher PCa was reached during the final meeting, the topic remained controversial during the online Delphi round, reflecting the lack of strong evidence in this area. Retrospective studies on FT outcomes for ISUP grade 3 PCa report conflicting results, with most studies including 20% or fewer patients with this grade [10, 25, 26]. For more aggressive diseases, data remains limited, although a few series have included a small subset of these patients [25, 26]. Solid oncological outcomes are still lacking, but treatments are already being performed, and more comprehensive data is expected to emerge in the near future.

In addition, there is uncertainty surrounding whether patients with intraductal and cribriform patterns should be considered for FT [27]. While there was a lack of consensus on whether or not the presence of cribriform and/or intraductal patterns are contraindications for FT, participants agreed that if cribriform pattern is present, FT should be considered over active surveillance for patients with localised ISUP 2 (percentage of pattern 4 <10%) PCa. The lack of consensus on this topic highlights an area where additional research is warranted. Another debated aspect of patient selection involves the consideration of patients with ECE on MRI. Participants agreed that FT should not be offered to patients when there is a likelihood of ECE observed on MRI. However, determining what constitutes a 'likelihood of ECE on MRI' may warrant further discussion, as this assessment could be influenced by MRI quality and radiologist interpretation. Furthermore, although the use of nomograms to predict the risk of ECE was not evaluated in the current Delphi consensus, they have demonstrated potential for improving the accuracy of ECE assessment [28]. Finally, there was a consensus that FT should not be offered if MRI is unavailable, negative, or of low quality. However, consensus remains elusive regarding whether PSMA PET imaging can serve as a substitute in cases where MRI is not feasible for the patient. Additionally, no consensus was reached on statement 25, which proposed that 'FT should not be offered in cases of negative

MRI and positive biopsies, even if mapping biopsy, as described by Winston Barzell, was performed.' These conflicting opinions highlight the urgent need for further research in these areas.

Concerning FT approach, there is debate about the optimal treatment margin when planning FT. One study found that for tumors up to 12 mm, a 6-mm margin achieved complete ablation of high-grade lesions; the authors concluded that a margin of 5-6 mm is adequate for tumors less than 12 mm [29]. Another study found that not all cancers were located within the MRI lesion, but 90% were within 10 mm of the lesions [30]. FALCON participants agreed that the minimal margin when treating a lesion is 5 mm and disagreed that the minimal margin is 10 mm, meaning that the optimal treatment margin lies within this range. For energy selection, results from FALCON indicated that no energy source can be recommended over others in terms of effectiveness and safety. Instead, energy selection should primarily be based on the location of the tumor (71% agreement) and the operator’s experience (77% agreement).

The timing and method for post-treatment monitoring and biopsies are not standardized. Participants in the FALCON project agreed that patients should be monitored for up to 10 years, PSA should be done 3 monthly for the first year, then 6 monthly, and MRI should be done yearly. Falcon proposed yearly MRI and its associated costs may be controversial, as this approach hasn't been proven superior to follow-up based on specific triggers (e.g., PSA elevation) or less frequent MRI schedules. Given the lack of robust evidence typical of Delphi studies, this proposal should be approached with caution. Additionally, variations in healthcare systems and participant realities may influence their responses. Similarly, regarding biopsies, 10-12 systematic plus 3-4 target biopsies should be done at 12 months post-treatment, and then only if there is clinical suspicion according to Falcon. However, the use of control biopsies varies worldwide, with some groups initially adopting them and discontinuing as they gain experience [31]. This underscores the need for clinical practice to be tailored not only to individual patient cases but also to the specific realities of healthcare centers, including access to high-quality MRI technology, expert interpretation, and experience in FT treatment, beyond Falcon's general recommendations.

Results from the FALCON project should be interpreted in light of several limitations. First, a systematic literature review was not conducted prior to developing the survey. Instead, a non-systematic review was performed and relied on previous systematic reviews and consensuses to create the survey. Second, while the goal was to recruit a diverse population of specialists in the

field of PCa treatment, almost 80% of participants in the third Delphi round were urologists. Third, with a 154-item initial questionnaire, the survey was time-consuming, and "respondent fatigue" may have negatively affected the results [32]. Fourth, 69 statements reached a consensus through the in-person meeting survey and discussion. It is likely that the views of this smaller group did not represent that of the larger respondent pool though the goal of this meeting was to achieve consensus through discussion when possible. Lastly, Delphi techniques are a lower levelfor evidence generation than clinical trials and well-designed observational studies. Therefore, these recommendations should be applied in conjunction with clinical judgment, and deviations from them are not necessarily detrimental to patient care or local policies. This is particularly important given the need for stronger evidence to transition from guidance to formal guidelines in the future. Additionally, as new data emerges, areas of consensus are likely to evolve, making this a dynamic field that requires continuous evaluation and periodic reassessment to ensure that the guidance stays aligned with the most up-to-date evidence.

Nevertheless, given the insufficiencies in the current literature, a broad international consensus statement appeared warranted. Moreover, registries now appear to be the most viable solution for obtaining robust oncological outcomes, given the high cost and feasibility challenges associated with trials. It is therefore crucial to reduce heterogeneity among patients included in ongoing registries, particularly since practitioners may lack standardized recommendations for performing FT. Without such standardization, interpreting results can become complex, bringing us back to the initial problem. The FALCON initiative aims to harmonize FT practices, minimize patient heterogeneity in registries, and enhance the likelihood of generating interpretable outcomes in the future. This ambitious objective represents the core goal of this extensive consensus effort.

In conclusion, the FALCON project, through an international Delphi consensus, provides comprehensive guidance on FT, covering key areas from patient selection to post-treatment follow-up. Furthermore, the project has highlighted significant gaps in the current evidence base, which could shape future research on FT and contribute to the development of more robust, evidence-based guidelines.

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Abbreviations

CAU	Confederacion Americana de Urologia
FALCON	FocAL therapy CONsensus
FT	focal therapy
FTS	Focal Therapy Society
ISUP	International Society of Urological Pathology
MRI	magnetic resonance imaging
PCa	prostate cancer
PSA	prostate-specific antigen
ECE	extracapsular extension
PSMA PET	prostate-specific membrane antigen positron emission tomography
SIU	Société Internationale d'Urologie

Tables

Table 1. Statements Not Reaching Consensus

Domain	Statement number	Statement
Patient selection: Biopsies	12	Prostate cancer diagnosis through transperineal biopsies is mandatory before FT.
Patient selection: MRI lesions and positive biopsies' location	21	FT may be offered to patients who cannot undergo MRI if it is replaced by PSMA.
	25	FT should not be offered in case of negative MRI and positive biopsies even if mapping biopsy as described by Winston Barzell was performed.
Patient selection: PSA level	71	Candidates for FT should have a PSA value ≤20ng/ml regardless of PSA density.
Patient selection: Local clinical stage on MRI	77	FT should only be considered if the clinical stage on MRI is ≤T2c.
Patient selection: Cribriform and intraductal patterns	86	The presence of cribriform and/or intraductal patterns are contraindications for FT.
Treatment Approach	108	The treatment of the lesion is insufficient and at least all prostate tissue within a quadrant of the prostate should be treated (quadrant ablation).
Treatment evaluation and follow-up	126	PSA failure after FT is nadir PSA+ 2 ng/dl.
	129	Follow-up with MRI and PSA is sufficient.
	131	Follow-up with PSMA imaging may be superior to MRI.
Future perspectives	145	In the next 5 years patients with oligometastatic disease may be candidates for FT.
	146	In the next 5 years locally advanced disease on the MRI will not be always a contraindication for FT.

FT = focal therapy; MRI = magnetic resonance imaging; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen