Ultrasound & Therapy

Information on Diagnostic and Therapeutic Ultrasound in Urology

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Bringing New Horizons to Therapy

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HIFU HIGH INTENSITY FOCUSED ULTRASOUND

Focal One® HIFU continues to gain momentum in the US

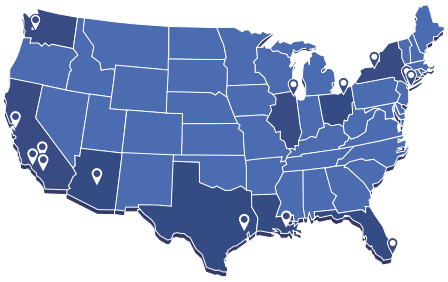
Focal·One®
ROBOTIC FOCAL HIFU

The Focal One® has gained significant momentum in the US since its FDA clearance in June 2018.

Receiving the Category I CPT® (Current Procedural Terminology) code for HIFU was an important milestone and continues to bring hospitals, doctors, and patients closer to reimbursement for HIFU. Today, hospitals, including some of the most highly ranked uro-oncology programs in the USA and in the world, have now acquired the Focal One® Robotic HIFU device, incorporating focal therapy in their therapeutic armamentarium.

Thanks to the concerted effort of the EDAP team in the deployment of their reimbursement strategy, HIFU was awarded the CPT code for HIFU just four months after filing the application, a process that could have taken at least two years. The support of the American Urological Association (AUA) and the American Association of Clinical Urologists (AACU) was instrumental in this process. And in the end, the American Medical Association (AMA) voted for the creation of a Cat. I CPT code for HIFU for the "Ablation of malignant prostate tissue, transrectal, with High Intensity Focused ultrasound (HIFU), including ultrasound guidance." Once the AMA approved the CPT Cat. I code, the AUA and AMA entered a survey process to define the appropriate payment level based on the time, complexity, level of expertise and experience required for a physician performing the HIFU procedure. The RUC panel reviewed and validated the defined relative value units (RVUs) and made a recommendation to CMS, which is responsible for issuing the official payment levels in the annual Medicare Physician Fee Schedule Rule. In the case of HIFU, despite a higher rate defined by the AMA RUC panel, CMS finalized a payment for a physician performing HIFU on a patient under Medicare around $1,000 as a national average (adjusted by a local wage index). Private insurances define a payment that is usually 1.6 to 2.8 times the Medicare payment. This CPT Cat. I code, effective since January 1, 2021, is a game changer in bringing hospitals, doctors and patients closer to reimbursement for HIFU. The insurer looks to the AMA for guidance and validation. With a dedicated CPT code, it is unequivocal that HIFU has been validated by the AMA and CMS, and is now perceived as a more "mainstream" option that brings patients, doctors and hospitals much closer to reimbursement. As a result, the number of HIFU procedures performed in the US with EDAP Robotic HIFU platforms in the first 6 months of 2021 with the new CPT code has increased 79% compared to the same period in 2020 in the absence of a CPT code.

Focal One® US centers



- Cleveland Clinic, OH
- Houston Methodist, TX
- Maimonides Medical Center, Brooklyn, NY
- Mayo Clinic, Phoenix, AZ
- Mt. Sinai Health System, New York, NY
- Ochsner Medical Center, New Orleans, LA
- P. St. John's Health/JohnWayne Cancer Institute, Santa Monica, CA
- Rochester Regional Health, NY
- University of California Irvine, CA
- University of California San Francisco, CA
- University of Chicago Medicine, IL
- University of Miami, FL
- University of S. California, Los Angeles, CA
- University of Washington, Seattle, WA

114e CONGRÈS FRANÇAIS D'UROLOGIE

AUA 2021

P/2 Encouraging data from the HiFi study presented during AFU 2020 & AUA 2021 congresses

GERMAN SOCIETY OF UROLOGY (DGU)

P/3 New Prostate Cancer German guidelines including Focal Therapy for the first time

SIU SOCIÉTÉ INTERNATIONALE D'UROLOGIE

DUBAI 2021
November 10-14

Thursday, November 11 - 07:30-09:00
Micro-Ultrasound/MRI Fusion Biopsy with Real Time Visualization
Dr Petr Macek - France

Focal One® Procedure
Prof. Franck Bladou - France

Friday, November 12 - 12:45-13:15 – RDT
Focal HIFU Therapy in PCa: Worldwide Practice Changes on the Horizon?
Chaired by Dr Sanchez Salas
Faculty: Prof. Pascal Rischmann - France and Prof. Martin Schostak - Germany

Encouraging data from the HiFi study presented during AFU 2020 & AUA 2021 congresses

114e CONGRÈS FRANÇAIS D'UROLOGIE

AUA 2021

The French Association of Urology (AFU) is the sponsor of the HIFI study within the framework of the "Forfait Innovation" (French Ministry of Health). This is a multicentric, prospective, non-randomized comparative study comparing, in a non-inferiority setting, HIFU (total or subtotal) vs radical prostatectomy (RP), in two populations: first-line and post-radiotherapy. This study, initiated and validated by the French Health Authority (HAS), will serve as a reference for decisions regarding the definitive reimbursement of HIFU treatments in France. The results summarized here are intermediate results from the first-line population.

From 2015 to 2019, 3364 patients were included in the primary treatment setting. Consistent with the CCAFU inclusion criteria, the HIFU population is significantly older (by more than 10 years). The two arms are comparable at baseline with a majority of Grade Group 2 and equivalent median PSA.

The intermediate analysis of carcinological data at 24 months, presented by Prof. Rischmann, shows:

- Principal criterion: significantly better survival in the HIFU group without salvage treatment* at 24 months (p<0.001)
- Secondary criteria: PSA nadir was 0.34 and 0.01ng/ml respectively. R1 rate after RP: 24%. Positive biopsies after HIFU: 8.6%

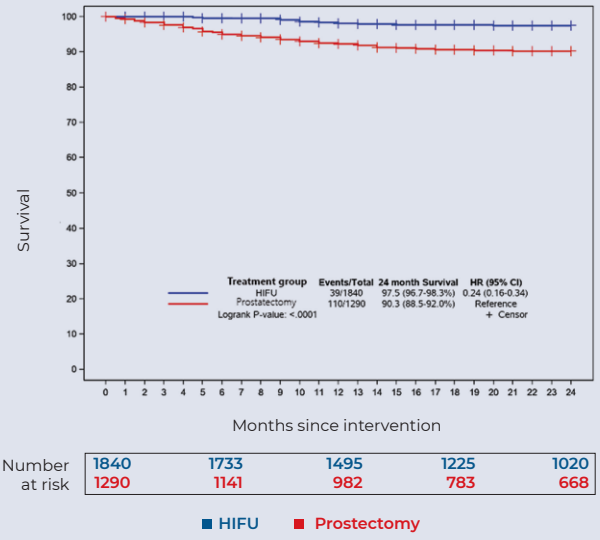
*The rate of salvage treatment (radiotherapy) after RP, validated in Oncological Committee, is influenced by the positive margin rate.

These are intermediate results not yet stabilized: 30-months follow-up is necessary.

The analysis of tolerance and safety at 12 months, presented by Dr Coloby, shows:

- 53 SAE were Clavien-Dindo ≥ IIIa: HIFU (1.6%) vs PT (1.5%). There were no early exit from the study due to SAE. Fistula rate: 0.15% in the HIFU arm vs 0.58% in the RP arm, all resolved.
- IPSS and IPSS QoL were equivalent in both groups.
- Urinary continence (USP) was significantly better in the HIFU group (p<0.005)
- Erectile function of patients aged 70 - 75 years (IEEF5 score ≥ 15 before treatment) was less impaired after HIFU vs RP (Δ = +1 vs - 9)
- Quality of life (EORTC QLQ-C30) was comparable (90.7 vs 93.4) in both groups, which have an age difference of 10.8 years.

Baseline characteristics and follow-up	HIFU	RP
Number of patients included, n	1988	1376
Median age	75.2	64.4
Median PSA (ng/mL)	7.1	6.9
ISUP1/ISUP2 (%)	41 / 59	37 / 63
Median PSA nadir (ng/mL)	0.34	0.01



In conclusion, no unforeseen risk were identified, no death were attributable to the studied interventions. The intermediate analysis at 24 months of the primary carcinological criterion shows **a significant difference in favor of the HIFU group**. The result is not consolidated; follow-up at 30 months is required. The HIFU group showed better functional results at 12 months. Post-treatment quality of life is comparable in both groups despite a significantly older population in the HIFU group.

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Bringing New Horizons to Therapy

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GERMAN SOCIETY OF UROLOGY (DGU)

New guidelines 2021 for Prostate Cancer including Focal Therapy for the first time

In Spring 2021, German Society of Urology (DGU) officially issued the new German S3 Guidelines regarding prostate cancer, and more specially, about the focal therapies place in the prostate cancer management. Until now, focal therapy was considered as highly experimental and only applicable in studies. Prof. Schostak presented in June in The One Club webinar the results: a 12 pages document, dedicated to focal therapy, based on current literature, describing the entire workflow from selection to follow-up and detailing the different techniques available. Now, in certain circumstances, focal therapy can be discussed. Prof. Schostak said "In Germany, only guidelines are able to lead to focal therapy to a broader acceptance, this first step is a very good basis for future updates and other guidelines in the next years".

THE ONE CLUB

10 sessions 290 participants connecting HIFU users

THE ONE CLUB

Focal One®

ROBOTIC FOCAL HIFU

The One Club has been created a year ago to maintain a link between HIFU users. Objective was to bring qualitative content and discussions to HIFU users through key speakers.

Today The One Club it's 10 webinars, 290 participants from all over the world, up to 110 connected people and a dedicated LinkedIn group. We are glad to see the path that has been made thanks to all our members. 10 One Club webinars have been conducted, thanks to HIFU users willing to share and discuss HIFU hot topics, among which we had:

- **France:** Prof. Rischmann sharing his intermediate results of HIFI study, the biggest French on-going study, comparing HIFU vs Prostatectomy, as a first line treatment for localized cancer treatement.
- **Germany:** Prof. Schostak presenting his work about German guidelines and the introduction of HIFU as a no longer experimental treatment technique.
- **USA:** Dr Abreu, detailing the first US publication about HIFU treatment with 100 American patients included.
- **Norway:** Dr Baco sharing intermediate results about FARP, the randomized study he's conducting to compare Focal HIFU vs Radical prostatectomy.
- And so many others to come with, for example, a future presentation of the first results of the Endometriosis study. So stay tuned!

The LinkedIn Group:
Launched in February, this additional The One Club tool has been thought as an extra exchange platform. Indeed webinars were great but with a limited time to exchange. The LinkedIn private group enables physicians to exchange and receive latest info about HIFU continuously.

If you're not yet a member, please contact us so that we'll send you an invitation: cnavarro@edap-tms.com.

MICRO-ULTRASOUND TARGETED BIOPSIES

Micro-Ultrasound and the Prostate Cancer Diagnostic Pathway

By Brian Wodlinger, PhD.

I am often asked how ExactVu™ micro-ultrasound fits into the diagnostic workflow for prostate cancer. This is a challenging question because, like all ultrasound, micro-ultrasound is a versatile tool with applications in several places along the pathway. However, several publications from the past year shed light on where micro-ultrasound may be useful. As a starting point, let's review the steps along the pathway. According to the 2021 v1 NCCN early detection guidelines[1], these are:

- **Baseline Evaluation, Risk Assessment, and Early Detection Evaluation (PSA and DRE)**
- **Further Evaluations and Indications for Biopsy (including biomarkers and MRI)**
- **Management (biopsy or follow-up)**

The 2021 v2 NCCN Prostate Cancer guidelines[2] pick up from here after a positive biopsy result with risk stratification to decide on treatment plans. Part of this risk stratification includes a determination of extraprostatic extension for staging of T1/2 vs. T3 disease.

Starting Early

Since mpMRI is recommended as a tool to help decide whether a man requires biopsy, it seems natural to question whether micro-ultrasound can be used for the same purpose. Like PI-RADS for MRI, micro-ultrasound has a dedicated risk stratification scale, PRI-MUS[3], and the risk levels appear to be similar between the two[4]. Recent data from Klotz et al. also showed improved negative predictive value (NPV) compared to MRI for this purpose in a large international cohort of 1,040 men[5]. This large study suffered from a lack of blinding of the MRI at some centers, although the authors note that the results at these centers were similar to the blinded centers. Similarly, the reference standard was not comparable to the rigorous template biopsy used in studies such as PROMIS[6]. A smaller blinded prospective single-site study may help mitigate these limitations. Socarrás et al. performed template "Mapping" biopsy after micro-ultrasound assessment and found that 27/194 men biopsied had low-risk PRI-MUS 2 prostates and 0/27 of these were positive for csPCa on mapping biopsy.

During Biopsy

Last year we had the first prospective, blinded, comparison of csPCa detection rate between MRI targeted biopsy and micro-ultrasound guided biopsy which demonstrated identical detection rates of csPCa[4]. This year, we add the first systematic review and meta-analysis confirming this result. Soutoulides et al.[7] included 13 studies with 1,125 participants receiving both micro-ultrasound and MRI targeted biopsy and concluded that the detection ratio for Grade Group ≥ 2 was nearly identical (1.05 with 95%CI 0.93-1.19). The detection ratio for insignificant (Grade Group 1) cancer was also very similar at 0.94 (95%CI 0.73-1.22). Finding significant prostate cancer is always the primary concern, however flexibility, overhead, and reducing harms are also important factors. With the release of a clip-in disposable transperineal guide, it is now very simple to transition from transrectal to transperineal biopsy using ExactVu. In the case of freehand transperineal biopsy, this can be done without any investment in new hardware. Transperineal biopsy can be performed under either local or general anesthesia and may provide a significant reduction in biopsy-related sepsis rates. The ExactVu system also comes with the FusionVu MRI-fusion feature, which allows you to easily incorporate MRI into your micro-ultrasound biopsy either using a full fusion approach with annotated MRIs or using the simpler Cognitive Assist feature from a standard PI-RADS report.

Planning Treatment

According to NCCN, the presence of T3 (extraprostatic) disease is sufficient to move a man into the High risk category, which may change management and will certainly inform surgical approach. In a small recent study Regis et al.[8] described the appearance of extraprostatic extension (EPE) on micro-ultrasound, demonstrating a sensitivity of 87.5% and specificity of 80%. The authors note this sensitivity is much higher than that of MRI (55-61%) with similar specificity (87-88%). These results confirm earlier work by Staerman[9] which also demonstrated that micro-ultrasound provided high sensitivity to detect EPE. In addition to staging and planning a surgical approach, micro-ultrasound has obvious applications in focal therapy. This technique is currently only accepted for salvage therapy, but is gaining traction for first line treatment as well under clinical trials and as an adjuvant to active surveillance. Micro-ultrasound may be of use here in identifying smaller satellite lesions which can change treatment plans by identifying secondary foci of significant disease and contralateral disease.[10]

Summary

There is growing evidence that micro-ultrasound can help at various points along the prostate cancer pathway, from informing the decision to biopsy, through the biopsy itself, and then with treatment planning. Some of the studies reviewed here are small and each has their own limitations. Larger well-controlled studies will be required before micro-ultrasound can be included in the clinical guidelines in each of these areas, but the consistency among these studies is very promising.

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