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1 **Novel volumetric and morphologic parameters derived from 3D virtual modelling to**
2 **improve comprehension of tumour's anatomy in patients with renal cancer.**

3
4 **Running head:** 3D parameters and renal anatomy

5
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1 **Keywords:** renal cancer; 3D modeling; 3D parameters; Robot-assisted partial
2 nephrectomy; complications

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1 **ABSTRACT**

2 **Background:** 3D models improve the comprehension of renal anatomy.

3 **Objective:** to evaluate the impact of novel 3D-derived parameters, to predict surgical
4 outcomes after Robot Assisted Partial Nephrectomy (RAPN).

5 **Design, Setting, and Participants:** 69 patients with cT1-T2 renal mass scheduled for
6 RAPN were included. 3D virtual modeling was achieved from computed tomography.
7 Following volumetric and morphological 3D parameters were calculated: V_T (volume of the
8 tumor); V_T/V_K (ratio between tumor volume and kidney volume); CSA_{3D} (i.e. Contact Surface
9 Area); UCS_{3D} (contact to the Urinary Collecting System); **Tumor-Artery_{3D}**: tumor's blood
10 supply by tertiary segmental arteries (*score*=1), secondary segmentary artery (*score*=2) or
11 primary segmentary/main renal artery (*score*=3); S_T (tumor's sphericity); **Conv_T**. (tumor's
12 convexity); **Endophyticity_{3D}** (ratio between the CSA_{3D} and the global tumor surface).

13 **Intervention:** RAPN with 3D model

14 **Outcome Measurements and Statistical Analysis:** 3D parameters were compared
15 between patients with and without complications. Univariate logistic regression was used to
16 predict overall complications and type of clamping; linear regression was used to predict
17 operative time, warm ischemia time and estimated blood loss.

18 **Results and limitations:** Overall, 11 (15%) individuals experienced overall complications
19 (7.2% had Clavien \geq 3 complications). Patients with UCS involvement at 3D model ($UCS_{3D}=2$),
20 tumor with primary or secondary segmental arteries supply (Tumor-Artery_{3D}=1 and 2) and
21 high Endophyticity_{3D} values had significantly higher rates of overall complications (all $p \leq$
22 0.03). At univariate analysis, UCS_{3D} , Tumor-Artery_{3D} and Endophyticity_{3D} are significantly
23 associated to overall complications; CSA_{3D} and Endophyticity_{3D} were associated to warm
24 ischemia time; CSA_{3D} was associated to selective clamping (all $p \leq 0.03$). Sample size and
25 the lack of interobserver variability are the main limits.

1 **Conclusion:** 3D modeling provides novel volumetric and morphological parameters to
2 predict surgical outcomes after RAPN.

3 **Patient Summary:** Novel morphologic and volumetric parameters can be derived from 3D
4 model to describe surgical complexity of renal mass and to predict surgical outcomes after
5 RAPN.

6

7

1 **INTRODUCTION**

2 Nephron sparing surgery (NSS) represents the treatment of choice for T1 Renal Cell
3 Carcinoma (RCC) regardless of the surgical approach^{1,2}. A critical and detailed
4 comprehension of renal anatomy and tumour's complexity is essential to achieve optimal
5 success of NSS. In the current era of precision surgery, the introduction of 3D modeling
6 technologies has brought significant improvements for comprehension of renal anatomy,
7 allowing a patient-tailored approach for NSS. Several nephrometry systems^{3,4,5,6,7,8} have
8 been proposed to objectively quantify the complexity of renal tumours and to predict surgical
9 complications. However, the current nephrometry scoring systems were assigned mainly by
10 visualization of two-dimensional (2D) imaging^{9,10} which is suboptimal for a complete
11 understanding of the morphological and anatomical features of renal mass and for planning
12 partial nephrectomy (PN). Of note, 3D models are navigable and enable to facilitate the
13 understanding of the size, location and depth of renal tumours, as well as the vascular and
14 collecting systems anatomy^{11,12}. Moreover, 3D models are more accurate to define the
15 surgical complexity of renal masses by nephrometry score than conventional 2D imaging¹².
16 Thus, 3D models allow to better plan the surgical approach to NSS and to increase the rate
17 of selective clamping^{11,13,14}. However, the potential applications of 3D modeling are not
18 totally investigated, and several information that can be derived from 3D virtual models and
19 their elaboration are still unexplored.

20 The aim of the present study was to identify and to define novel volumetric and morphologic
21 parameters derived from anatomical 3D modeling, and to evaluate the impact of these
22 features to predict surgical outcomes after Robot Assisted PN (RAPN).

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1 **MATERIALS AND METHODS**

2 *Study design and participants*

3 We prospectively enrolled 69 consecutive patients with organ-confined (cT1-T2) renal mass,
4 referred to RAPN at our Institution between January 2019 and March 2020. Participants
5 signed a written informed consent document. The study was approved by our Institutional
6 Ethics Committee (IRB approval 3386/2018). Before surgery, patients were addressed to
7 undergo 3D virtual modelling from preoperative computed tomography (CT) scan. The
8 surgeon reviewed both the 2D CT imaging and the 3D virtual models before and during
9 RAPN to guide the surgical planning and to improve anatomic knowledges during surgery.

10

11 *3D modeling*

12 To obviate bias due to inaccurate 2D preoperative imaging, before surgery all patients
13 underwent high quality chest and abdominal contrast-enhanced CT at our Institution (slice
14 thickness: 1.25 ÷ 2.5 mm, step interval: 0.8÷ 2.0 mm). All 3D virtual model reconstructions
15 based on preoperative high-CT scan, were carried out by engineers at eDIMES Lab of the
16 University of Bologna (IRCCS, Azienda Ospedaliero-Universitaria, S. Orsola-Malpighi
17 Hospital), as previously described^{11,15,16}.

18 Briefly, multiple imaging series with different contrast levels were used for the selective
19 identification of each anatomical structure of interest (healthy renal parenchyma, renal
20 tumour, arterial tree, renal veins, urinary collecting system [UCS]) in the image segmentation
21 process. Segmentation, i.e. the labelling of each structure of interest in CT images was
22 achieved using D2P™ software ('DICOM to PRINT'; 3D Systems Inc., Rock Hill, SC). The
23 segmented anatomical structures arising from the multiple imaging series were then
24 combined into one file using alignment of common regions, such as the healthy renal
25 parenchyma that was segmented in all the series. The segmentation process, which is a
26 semiautomatic procedure requiring both good knowledge of the anatomy and deep expertise

1 in medical image processing, was performed by engineers, who worked in close interaction
2 with surgeons and radiologists for reviewing the segmentation results and the anatomical
3 correctness of the reconstructed 3D virtual models¹⁴

4

5 *Surgical technique*

6 PNs were performed with robot-assisted approach by a single expert surgeon (RS). DaVinci
7 Xi platform with four arms, as previously described^{11,14}. In case of clamping approach to the
8 renal hilum we adopted warm ischemia: a selective (first segmental branch) or super-
9 selective (second and tertiary segmental branch) clamping approach was preferred
10 whenever feasible according to preoperative imaging and intraoperative patients-specific
11 surgical anatomy^{11,15}.

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14 3D-derived parameters

15 Three expert bioengineers (EM, LC and BB) and three urologists (LB, AM and SB) with
16 experience with nephrometry, calculated the following volumetric and morphological 3D
17 parameters of the renal mass on the basis of the obtained 3D virtual models, using
18 Meshmixer (Autodesk Inc, San Rafael, CA) and Excel (Microsoft Corp., Redmond,
19 Washington, US) software: V_T [cm³] (i.e. volume of the tumor); V_T/V_K (i.e. ratio between the
20 tumor volume and the ipsilateral kidney volume); **Tumor-Artery_{3D}**: cortical tumor with blood
21 supply by tertiary segmental arteries (*score*=1), medullary tumor with blood supply by
22 secondary segmentary artery (*score*=2) and hilar tumor with blood supply by primary
23 segmentary or main renal artery (*score*=3) based on univariate logistic regression analysis
24 to predict overall complications; S_T (i.e. sphericity of the tumor): continuous parameter to
25 quantify how closely the shape of the tumor approaches that of a mathematically perfect
26 sphere ($S_T=1$); **Conv_r**: (i.e. convexity of the tumor): continuous parameter to quantify the

1 regularity of tumor 3D morphology, obtained as ratio between the tumor volume and the
2 smallest volume that fully encloses it, and that is convex at all points; **CSA_{3D}** (i.e. Contact
3 Surface Area [cm²]); **UCS_{3D}** (i.e. contact of the tumor to the UCS; no contact with UCS
4 [score=1], contact/dislocation/invasion of UCS [score=2] based on univariate logistic
5 regression analysis to predict overall complications); **Endophyticity_{3D}**: ratio between the
6 CSA_{3D} and the global tumor surface: it is an index of the tumor endophyticity, as evaluated
7 from the 3D model.

8 The 3D-derived parameters are described in detail in Table 1 and depicted in Figures 1-2.

9

10 *Covariates*

11 Intraoperative data including overall operative time, type of resection (simple enucleation vs.
12 standard PN), level of arterial clamping (totally clampless vs. non-selective [i.e., clamping of
13 main renal artery] vs. selective clamping [i.e., clamping of primary, secondary or tertiary
14 segmental arteries]), time of defatting, time of hilar dissection, time of ischemia, time of
15 resection and intraoperative complications were recorded. Postoperative data included
16 length of hospital stay, haemoglobin, serum creatinine and eGFR at discharge, and 30- and
17 90-day postoperative complications, defined as any postoperative event altering the normal
18 post procedural course and/or delaying discharge and/or caused readmission, and were
19 classified according to the Dindo modification of the Clavien system¹⁷ and Comprehensive
20 Complication Index (CCI)¹⁸.

21

22 *Outcomes*

23 The primary outcome of the study was to investigate whenever the proposed novel
24 volumetric and morphologic parameters derived from anatomical 3D modeling may predict
25 surgical outcomes in patients underwent RAPN (including, overall complications, operative
26 time, warm ischemia time and estimated blood loss).

1

2 *Statistical analyses*

3 First, Chi-squared test, T-student test and Mann-Whitney U-test were used to compare
4 proportions, means and medians of volumetric and morphological 3D parameters between
5 patients with and without postoperative complications after RAPN. Second, to evaluate the
6 association between the proposed volumetric and morphological 3D parameters (namely,
7 **V_T** , **V_T/V_K** , **CSA_{3D}** , **UCS_{3D}** , **$Tumor-Artery_{3D}$** , **S_T** , **$Conv_T$** and **$Endophyticity_{3D}$**) and the
8 occurrence of overall complications and clamping approach we performed univariate logistic
9 regression analysis, while linear regressions were used to test the association with operative
10 time, warm ischemia time and estimated blood loss.

11 Finally, to produce curve representing the probability to experience overall complications
12 over **$Endophyticity_{3D}$** , LOESS plots were produced using mean value of **$Endophyticity_{3D}$**
13 to estimate overall complications predicted by linear regression analysis. All statistical tests
14 were performed using the Statistical Package for Social Sciences software, v.26.0 (SPSS
15 Inc., Chicago, IL, USA) with a 2-sided significance level set at $p < 0.05$.

16

17

1 **RESULTS**

2 Overall, 55 (79.7%), 13 (18.8%) and 1 (1.5%) patients had cT1a, cT1b, cT2a renal cancer,
3 respectively (Table 2). The intraoperative adopted clamping approach was clampless, non-
4 selective (main artery), selective (first segmental artery) and super-selective (second or third
5 segmental artery) in 23 (33.3%), 19 (27.5%), 24 (34.8%) and 3 (4.3%) cases, respectively
6 (Table 3). During surgery, two (2.9%) intraoperative complications were observed. Overall,
7 10 (14.4%) patients experienced postoperative complications (all Clavien grade ≤ 3) with
8 mean CCI of 6.9. Supplementary Table 1 shows the type and grade of any overall
9 complication. Patients with high PADUA score risk ($p=0.03$), UCS involvement at 3D model
10 (***UCS_{3D}***=2, $p=0.02$), tumor with primary or secondary segmental arteries supply (***Tumor-***
11 ***Artery_{3D}***=2 and 3, respectively, $p=0.02$) and high ***Endophyticity_{3D}*** values ($p=0.03$) had
12 significantly higher rates of overall complications (Table 4). At univariate logistic regression,
13 ***UCS_{3D}*** (OR: 4.59), ***Tumor-Artery_{3D}*** (OR: 3.50) and ***Endophyticity_{3D}*** (OR: 1.04) are
14 significantly related to any overall complications; ***CSA_{3D}*** (OR: 0.49) and ***Endophyticity_{3D}***
15 (OR: 0.12) were associated to warm ischemia time; ***CSA_{3D}*** (OR: 0.92) was associated to
16 selective clamping (all $p \leq 0.03$; Supplementary Table 2); Supplementary Figure 1 depicts
17 the linearity of the association of ***Endophyticity_{3D}*** with complications ($p=0.03$).

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1 **DISCUSSION**

2 Beside tumor's size¹⁹, different characteristics, including location, renal sinus involvement,
3 relationship with UCS, contact with renal surface and vascular anatomy, should be carefully
4 evaluated before planning PN to predict surgical complexity and the effectiveness of PN
5 rather than radical nephrectomy. As consequence, different renal nephrometry
6 scores^{5,6,7,20,21} have been introduced to better standardize tumor's characteristics. Which
7 nephrometry system is the most accurate to predict surgical complexity and better outcomes
8 of PN²², is still matter of debate. Of note, RENAL and PADUA score, which are easy to
9 calculate by using 2D CT scan images and have a good association with most outcomes,
10 are the most popular in literature²³. Of note, CT scan images are easily available, however,
11 2D imaging could be inaccurate to precisely define the relationship of renal mass with nearby
12 kidney's structures. Indeed, 2D images are unable to identify the exact intrarenal vascular
13 anatomy and to predict the real tumour blood supply from segmental branches¹³. Thus, the
14 adoption of 3D virtual model can be used as additional tools to improve the understanding
15 of renal anatomy before PN^{11,24}. As consequence, the high-fidelity 3D reconstruction of renal
16 vasculature allows to increase the adoption of selective clamping^{11,24}.

17 Moreover, previous authors¹² stated that 3D-based PADUA and RENAL scores better define
18 the complexity of renal mass and had higher predictive accuracy for postoperative
19 complications compared to nephrometry scoring system based on 2D imaging.

20 However, the potential applications of 3D modelling are not totally investigated, and several
21 information that can be derived from 3D virtual models and their elaboration are still
22 unexplored. Indeed, we identified novel morphologic and volumetric parameters derived
23 from 3D models.

24 Several results are remarkable. First, we report for the first-time novel 3D features to define
25 the complexity of renal mass in standard manner, and we provide a comprehensive
26 evaluation of the impact of the proposed 3D-derived parameters to predict surgical

1 outcomes after RAPN. Second, V_T , V_T/V_K , S_T , $Conv_T$, CSA_{3D} and $Endophyticity_{3D}$ are
2 numeric parameters based on 3D features with objective description and lower potential
3 reporting error compared to visual parameters based on 2D imaging; UCS_{3D} and $Tumor-$
4 $Artery_{3D}$ are visual parameters, but the assessment based on 3D models increases the
5 precision to define relationship between the tumor and the collecting system and arterial
6 branches compared to conventional 2D imaging.

7 Moreover, they can be easily calculated using Meshmixer software and Excel calculator
8 spreadsheet, out of additional costs, and they are generalizable and standardize for
9 scientific report thus allowing effective comparison with different cases.

10 Third, among all novel proposed 3D parameters to characterize renal mass and to evaluate
11 complication after NSS, the volume of the tumor, the ratio between the tumor volume and
12 the ipsilateral kidney volume, the sphericity of the tumor, the convexity of the tumor and the
13 CSA, all based on 3D model, were comparable between patients who experienced
14 complications and those who did not. However, patient with UCS involvement ($p=0.02$),
15 tumor with primary or secondary segmental arteries supply ($p=0.02$) and higher
16 Endophyticity ($p=0.03$) calculated on the 3D model, had significantly higher rates of overall
17 complications. Similarly, UCS_{3D} , $Tumor-Artery_{3D}$ and $Endophyticity_{3D}$ are significantly
18 associated to any complications at univariate logistic regression.

19 These data confirmed that UCS involvement is a crucial characteristic in predicting overall
20 complications after PN since urinary leakage represents one of most diffuse complications
21 (4.3% in our cohort) in case of close relationship between the tumor and the collecting
22 systems. The segmental arteries supply, based on 3D rendering of arterial branches
23 evaluated on 3D model, is useful tools to plan effective clamping PN. Moreover, tumors with
24 blood supply from main artery or first segmental arteries are more suitable for complications
25 due to centrally located mass, at higher risk of renal bleeding (6.2% in the overall population)
26 or urinary leakage. The $Endophyticity_{3D}$ aims to replace the categorized endophytic rate

1 (namely, $\geq 50\%$, $<50\%$ and endophytic) as depicted in RENAL⁶ and PADUA⁵ score that
2 suffer from inaccurate evaluation by 2D imaging and difficult evaluation of border-line cases:
3 the objective numeric expression from 3D evaluation as continuous variable suggests that
4 20-points increase in ***Endophyticity_{3D}*** has a significant impact to predict complication after
5 RAPN (Supplementary Figure 1).

6 The 3D derived features provide additional volumetric and morphological parameters, that
7 could not be evaluated in 2D images, and may be useful to objectively characterize, to report
8 and to understand the complexity of renal tumors and to predict complications, thus helping
9 surgeons during planning of the surgical approach. However, the quality of CT scan used
10 for 3D model reconstruction should be high-quality with slice thickness ≤ 2.5 mm, otherwise
11 the precision of 3D model is inadequate to be reliable for surgical navigation.

12 Finally, the proposed innovative 3D derived parameters may be useful to create further 3D-
13 based nephrometry scores to predict outcomes of PN.

14 Despite several strength, our study is not avoided from limitations. First the sample size is
15 limited, however the prospective nature of the study may mitigate this limitation.

16 Second, the inclusion of 3 urologists and 3 bioengineers for the evaluation of these
17 parameters could be biased by interobserver variability.

18 Third, most nephrometry scores and parameters were ideated to predict outcomes and
19 complications of open PN; all cases included in our cohort underwent RAPN, so the adoption
20 of robotic approach could have reduced the occurrence of postoperative complications.

21 Fourth, in our experience 3D models are not routinely used in every cases due to several
22 issue: engineers should have experience in using certified software for medical image
23 segmentation and they need strict collaboration with radiologists and urologist for reviewing
24 the images and validating the model, 3D reconstruction may take from 2 to 3 hours and it
25 costs approximately 100 euros per single reconstruction, considering the software licence
26 fee and costs for human resources. However, increasing evidence suggest the importance

1 of 3D models for several utilities during PN, giving the chance to even more diffusion in the
2 future and to improve automated segmentation algorithms, thus reducing costs and
3 increasing accuracy related to this technology.

4 Further perspective may include the proposed 3D-derived anatomic and morphologic
5 parameters in a novel 3D-specific nephrometry score to standardize the surgical complexity
6 of renal mass and to better predict surgical outcomes of NSS.

7

1 **CONCLUSION**

2 The use of computerized software for processing 3D models can be used to extrapolate
3 objective and standardized features to describe surgical complexity of renal tumour: volume
4 of the tumor, ratio between the tumor volume and the ipsilateral kidney volume, sphericity
5 of the tumor, convexity of the tumor, CSA, UCS involvement, arterial tumor's supply and
6 Endophyticity. Of note, UCS_{3D} involvement, arterial tumor's supply_{3D} and Endophyticity_{3D}
7 are significantly associated ~~correlated~~ with overall complications after RAPN, while only
8 CSA_{3D} and Endophyticity_{3D} were associated to warm ischemia time and CSA_{3D} was
9 associated to selective clamping.

10

1 **Disclosure of potential conflicts of interest**

2 The authors declare that they have no conflict of interest.

3

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1 **Research involving Human Participants and/or Animals**

2 All procedures performed in studies involving human participants were in accordance with
3 the ethical standards of the Institutional research committee (Comitato Etico di Area Vasta
4 Emilia Centro, Policlinico Sant'Orsola-Malpighi, Bologna, Prot. N. 323) and with the 1964
5 Helsinki declaration and its later amendments or comparable ethical standards.

6

1 **Figure legend**

2 **Figure 1.** a) Tumour Volume (V_T), in green, and kidney volume (V_K), in grey, as derived from
3 the 3D models. b) UCS_{3D} index calculated from the 3D models: it categorizes the contact of
4 the tumour with the urinary collecting system (UCS). In this example, two different scores of
5 UCS_{3D} index are shown. c) Tumor-Artery $_{3D}$ index calculated from the 3D models: it
6 categorizes how the tumour is in close proximity to the arterial vessels. In this example,
7 three different scores of Tumor-Artery $_{3D}$ index are shown (Score 1: blood supply by tertiary
8 segmental arteries; Score 2: blood supply by secondary segmentary artery; Score 3: supply
9 by primary segmentary or main renal artery)

10

11 **Figure 2.** a) Tumour sphericity index (S_T) calculated from the 3D model: it quantifies how
12 closely the shape of the tumour approaches that of a perfect sphere. In this example, two
13 different values of S_T index are shown. b) Tumour convexity index ($Conv_T$) calculated from
14 the 3D model: it quantifies the regularity of tumour 3D morphology, i.e. how it approaches
15 to a convex (i.e. with no concavities) shape. In this example, two different values of the
16 $Conv_T$ index are shown. c) CSA index calculated from 3D model (CSA_{3D}): it corresponds to
17 the surface of the endophytic part of the tumour (orange part in the figure); d) Endophyticity $_{3D}$
18 index calculated from the 3D model: it corresponds to the ratio between the CSA_{3D} and the
19 global surface area of the tumour (SA_T) represented in blue in the figure. In this example,
20 two different values of the tumour Endophyticity $_{3D}$ index are shown.

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1 **Supplementary Figure 1.** Predicted probability of overall complications (solid graph) and
2 95% confidence intervals (dotted graphs) is plotted against Endophyticity_{3D} by linear
3 regression analysis of mean value of Endophyticity_{3D} value.

4

1 **References**

- 2 1. Schiavina R, Mari A, Bianchi L, et al. Predicting positive surgical margins in partial
3 nephrectomy: A prospective multicentre observational study (the RECORD 2
4 project). *Eur J Surg Oncol*. 2020;46(7). doi:10.1016/j.ejso.2020.01.022
- 5 2. Borghesi M, Schiavina R, Gan M, Novara G, Mottrie A, Ficarra V. Expanding
6 utilization of robotic partial nephrectomy for clinical T1b and complex T1a renal
7 masses. *World J Urol*. 2013;31(3):499-504. doi:10.1007/s00345-013-1095-2
- 8 3. Simmons MN, Ching CB, Samplaski MK, Park CH, Gill IS. Kidney tumor location
9 measurement using the C index method. *J Urol*. 2010;183(5):1708-1713.
10 doi:10.1016/j.juro.2010.01.005
- 11 4. Hakky TS, Baumgarten AS, Allen B, et al. Zonal NePhRO scoring system: a superior
12 renal tumor complexity classification model. *Clin Genitourin Cancer*. 2014;12(1):e13-
13 8. doi:10.1016/j.clgc.2013.07.009
- 14 5. Ficarra V, Novara G, Secco S, et al. Preoperative aspects and dimensions used for
15 an anatomical (PADUA) classification of renal tumours in patients who are
16 candidates for nephron-sparing surgery. *Eur Urol*. 2009;56(5):786-793.
17 doi:10.1016/j.eururo.2009.07.040
- 18 6. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive
19 standardized system for quantitating renal tumor size, location and depth. *J Urol*.
20 2009;182(3):844-853. doi:10.1016/j.juro.2009.05.035
- 21 7. Ficarra V, Porpiglia F, Crestani A, et al. The Simplified PADUA REal (SPARE)
22 nephrometry system: a novel classification of parenchymal renal tumours suitable
23 for partial nephrectomy. *BJU Int*. April 2019. doi:10.1111/bju.14772
- 24 8. Schiavina R, Novara G, Borghesi M, et al. PADUA and R.E.N.A.L. nephrometry
25 scores correlate with perioperative outcomes of robot-assisted partial nephrectomy:
26 analysis of the Vattikuti Global Quality Initiative in Robotic Urologic Surgery (GQI-

- 1 RUS) database. *BJU Int.* 2017;119(3):456-463. doi:10.1111/bju.13628
- 2 9. Righi V, Mucci A, Schenetti L, et al. Ex vivo HR-MAS magnetic resonance
3 spectroscopy of normal and malignant human renal tissues. *Anticancer Res.*
4 2007;27(5A):3195-3204.
- 5 10. Schiavina R, Borghesi M, Chessa F, et al. The Prognostic Impact of Tumor Size on
6 Cancer-Specific and Overall Survival among Patients with Pathologic T3a Renal Cell
7 Carcinoma. *Clin Genitourin Cancer.* 2015;13(4). doi:10.1016/j.clgc.2014.06.011
- 8 11. Bianchi L, Barbaresi U, Cercenelli L, et al. The Impact of 3D Digital Reconstruction
9 on the Surgical Planning of Partial Nephrectomy: A Case-control Study. Still Time
10 for a Novel Surgical Trend? *Clin Genitourin Cancer.* April 2020.
11 doi:10.1016/j.clgc.2020.03.016
- 12 12. Porpiglia F, Amparore D, Checcucci E, et al. Three-dimensional virtual imaging of
13 renal tumours: a new tool to improve the accuracy of nephrometry scores. *BJU Int.*
14 August 2019. doi:10.1111/bju.14894
- 15 13. Schiavina R, Bianchi L, Borghesi M, et al. Three-dimensional digital reconstruction of
16 renal model to guide preoperative planning of robot-assisted partial nephrectomy. *Int*
17 *J Urol.* June 2019. doi:10.1111/iju.14038
- 18 14. Schiavina R, Bianchi L, Chessa F, et al. Augmented Reality to Guide Selective
19 Clamping and Tumor Dissection During Robot-assisted Partial Nephrectomy: A
20 Preliminary Experience. *Clin Genitourin Cancer.* 2020.
21 doi:10.1016/j.clgc.2020.09.005
- 22 15. Schiavina R, Bianchi L, Borghesi M, et al. Three-dimensional digital reconstruction of
23 renal model to guide preoperative planning of robot-assisted partial nephrectomy. *Int*
24 *J Urol.* 2019;26(9). doi:10.1111/iju.14038
- 25 16. Bianchi L, Schiavina R, Barbaresi U, et al. 3D reconstruction and physical renal
26 model to improve percutaneous puncture during PNL. *Int Braz J Urol.* 2019;45(6).

1 doi:10.1590/S1677-5538.IBJU.2018.0799

- 2 17. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new
3 proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann*
4 *Surg.* 2004;240(2):205-213. doi:10.1097/01.sla.0000133083.54934.ae
- 5 18. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien P-A. The comprehensive
6 complication index: a novel continuous scale to measure surgical morbidity. *Ann*
7 *Surg.* 2013;258(1):1-7. doi:10.1097/SLA.0b013e318296c732
- 8 19. Kriegmair MC, Mandel P, Moses A, et al. Defining Renal Masses: Comprehensive
9 Comparison of RENAL, PADUA, NePhRO, and C-Index Score. *Clin Genitourin*
10 *Cancer.* 2017;15(2):248-255.e1. doi:10.1016/j.clgc.2016.07.029
- 11 20. Leslie S, Gill IS, de Castro Abreu AL, et al. Renal tumor contact surface area: a
12 novel parameter for predicting complexity and outcomes of partial nephrectomy. *Eur*
13 *Urol.* 2014;66(5):884-893. doi:10.1016/j.eururo.2014.03.010
- 14 21. Spaliviero M, Poon BY, Karlo CA, et al. An Arterial Based Complexity (ABC) Scoring
15 System to Assess the Morbidity Profile of Partial Nephrectomy. *Eur Urol.*
16 2016;69(1):72-79. doi:10.1016/j.eururo.2015.08.008
- 17 22. Bianchi L, Schiavina R, Borghesi M, et al. Which patients with clinical localized renal
18 mass would achieve the trifecta after partial nephrectomy? The impact of surgical
19 technique. *Minerva Urol Nefrol.* October 2019. doi:10.23736/S0393-2249.19.03485-
20 4
- 21 23. Veccia A, Antonelli A, Uzzo RG, et al. Predictive Value of Nephrometry Scores in
22 Nephron-sparing Surgery: A Systematic Review and Meta-analysis. *Eur Urol Focus.*
23 2020;6(3):490-504. doi:10.1016/j.euf.2019.11.004
- 24 24. Porpiglia F, Fiori C, Checcucci E, Amparore D, Bertolo R. Hyperaccuracy Three-
25 dimensional Reconstruction Is Able to Maximize the Efficacy of Selective Clamping
26 During Robot-assisted Partial Nephrectomy for Complex Renal Masses. *Eur Urol.*

1 2018;74(5):651-660. doi:10.1016/j.eururo.2017.12.027

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