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Accuracy of implementing principles of fusion imaging in the follow up and surveillance of complex aneurysm repair

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Complete List of Authors:	Martin-Gonzalez, Teresa; Royal Free London NHS Foundation Trust, Vascular Surgery Penney, Graeme; King's College London School of Medical Education, Engineering Chong, Debra; Royal Free London NHS Foundation Trust, Vascular Surgery Davis, Meryl; Royal Free Hospital, Royal Free London NHS Foundation Trust; Mastracci, Tara; Royal Free Hospital, Royal Free London NHS Foundation Trust
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Abstract:	Fusion imaging is standard for the endovascular treatment of complex aortic aneurysms, but its role in follow-up has not been explored. A critical issue is renal function deterioration over time. Renal volume has been used as a marker of renal impairment , however it is not reproducible and remains a complex and resource-intensive procedure. The aim of this study is to determine the accuracy of a fusion-based software to automatically calculate the renal volume changes during follow-up. In this study, CT scans of 16 patients who underwent complex aortic endovascular repair were analysed. Preoperative, 1-month and 1-year follow-up CT scans have been analysed using a conventional approach of semiautomatic segmentation, and a second approach with automatic segmentation. For each kidney and at each time point the percentage of change in renal volume was calculated using both techniques. After review, volume assessment was feasible for all CT scans. For the left kidney, Interclass Correlation Coefficient (ICC) was 0.794 and 0.877 at 1-month and 1-year, respectively. For the right side, ICC was 0.817 at 1 month and 0.966 at 1 year. ~~For the >60% scans, the~~ automated technique reliably detected a decrease in renal volume for patients with occluded renal arteries during follow-up. This is the first report of a fusion-based algorithm to detect changes in renal volume during post operative surveillance using an automated process. Using this technique, the standardised assessment of renal volume could be implemented with greater ease and reproducibility and serve as a warning of potential renal impairment.

Accuracy of implementing principles of fusion ~~imaign gin~~ the follow up and surveillance of complex aneurysm repair ~~Feasibility of implementing principles of Fusion imaging in the Follow-up of Complex Aneurysm Repair~~

T Martin-Gonzalez[1], G Penney[2], Chong D[1], M Davis[1], TM Mastracci[1]

[1]Royal Free Hospital, London, UK

[2]CYDAR imaging, Cambridge, UK/Imperial College, London, UK

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Corresponding Author,

TM Mastracci

Clinical Lead, Aortic Surgery

Royal Free London

Pond Street

London, UK

NW3 2QG

tara.mastracci@nhs.net.

Introduction

The endovascular treatment of complex aneurysm has evolved as an alternative to open repair (1) and it has become standard of care in many jurisdictions. Although outcomes are durable(2)(3)(4)(5), renal impairment during follow up is still a critical issue, and difficult to quantify. Many different markers, such as renal volume, stent angulation, and stent stenosis, have been used to predict renal impairment. (6)(7)(4) Using a combination of these variables is not a reproducible method to assess renal impairment, despite being a complex and resource-intensive process.

Advanced imaging techniques such as 3D fusion significantly reduces radiation exposure and contrast utilization in EVAR as well as in complex endovascular procedures (8). However utilizing the principles of fusion imaigngimaging in follow-up has not been explored. The aim of this study is to determine the accuracy of fusion-based techniques to automatically calculate the renal volume changes during follow-up with automated segmentation software, and standardise its use.

Material and Methods

Study population. We selected CT scans of 16 patients who went under complex aortic endovascular repair in our centre to include in this analysis. This group included 8 patients who underwent FEVAR with no complications throughout follow-up, and 8 patients who sustained at least one renal occlusion during follow-up. We assumed that renal occlusion would be the most dramatic event leading to renal volume change. The patients were drawn from the local experience of cases performed between 2012 and 2016. Inclusion required a renal event with at least one CT scan after the event occurred. Controls were chosen to match patients with renal events. Demographics of both are included in table I.

Retrospectively both preoperative, 1-month and 1-year follow-up CT scans were analysed using a conventional approach of semiautomatic segmentation in conventional software, and using a second approach exploring new software with automatic segmentation. The rationale behind analysing serial images is to determine the degree of accuracy this method has in assessing change in renal volume, as it is well established that ~~devascularziation~~devascularisation of a kidney leads to progressive shrinkage of the kidney over time. Ethical approval of the local institution was waived as this is a retrospective observational study.

Renal function. The eGFR was determined by the abbreviated MDRD study equation (eGFR [ml x min^{-1} x 1.73 m^{-2}] = 186 x [serum creatinine]$^{-1.154}$ x [age]$^{-0.203}$ x [0.704 if female] x [1.210 if African American]). The eGFR was calculated preoperatively, at 1 month and at 1-year follow-up.

Imaging analysis. Using the conventional system, CTs were interrogated using a multiplanar three-dimensional workstation (AquariusNet software, TeraRecon Inc, San Mateo, Calif). Renal events were agreed by two investigators. The volume of each kidney was calculated with the following method: after selection of an area of interest, a ~~semiautomated~~semi automated post-processing algorithm extracted the renal contour based on pixels of similar attenuation; the pelvicalyceal system, fat and vessels in the renal sinus, and renal cysts were excluded by manual correction on multiplanar views (to correct for any confounding automatic inclusion); finally, the renal volume was estimated with an algorithm embedded in the software package (in cubic centimetres) (Figure 1). The robustness of this method has been published in a

previous study (9). Predicted postoperative eGFR was calculated by renal volume change using the equation developed by Shimoyama et al (10): *predicted postoperative eGFR= preoperative eGFR x (postoperative renal volume/preoperative renal volume)*. The correlation between the predicted and the observed postoperative eGFR has been quantified.

An overview of the new fusion-based method is shown in ~~figure~~ 2. The operator used the itksnap image viewer (www.itksnap.org)(11) to manually select 6 points in the preoperative CT and a single point in the postoperative CT. These points were used to provide a starting position and region-of-interest for the automatic fusion algorithm.

The algorithm then proceeds automatically and iteratively translates, rotates and scales the postoperative CT and compares it with the preoperative image of the kidney. The images are compared using a statistical measure (correlation coefficient) applied to the underlying voxel intensity values. When an optimum fusion is achieved the postoperative kidney will be positioned and scaled so it closely resembles the preoperative kidney. The amount of scaling applied to fuse the images is a measurement of change in kidney size – the scaling occurs automatically in two dimensions and the degree of change is calculated by the programme. In the example shown the algorithm increased the size of the postoperative kidney by a factor of 1.81 to accurately fuse with the preoperative kidney. Alternatively this could be stated as: the postoperative kidney has shrunk to 55% (1/1.81) of its preoperative volume.

For each kidney and at each time point the percentage of change in renal volume compared to the preoperative one has been calculated using both techniques and the reliability of ratings has been assessed.

Statistical analysis. Statistical analysis was performed in SPSS version 20 (Statistical Package Social Sciences Inc., Chicago, IL, USA). Descriptive statistics were generated, and the correlation between predicted and observed eGFR was calculated with the Pearson correlation. The reliability of ratings has been assessed with the interclass correlation coefficient and the Pearson correlation. The test value was defined as $p< 0.05$.

Results

Table 1 summarizes the demographic characteristics of the 16 patients included in the study, divided by group. The median preoperative eGFR was 80.5 ml/min [49.25-89.75] in the group without renal occlusion during follow up and 55 ml/min [42.25-74.50] in the occlusion group. Renal volume assessment was feasible for all CT scans included in the study. Correlation between predicted eGFR, based on renal volume calculated with the ~~semiautomated~~semi automated process, and observed eGFR was r=0.844 ~~(p< 0.000)~~ is depicted in ~~figure~~ 3. Divided into non-occlusion and occlusion group, the correlation was r=0.899 (p=0.001) and r=0.800 (p=0.031) respectively.

We assessed the reliability of both analysis techniques using the Interclass Correlation Coefficient (ICC). For the left kidney, the ~~Interclass Correlation Coefficient (ICC)~~ was 0.794 and 0.877 at 1-month and 1-year follow-up, respectively. For the right side, at 1-month the ICC was 0.817 and 0.966 at 1-year. For each kidney and at each time point, the Pearson correlation coefficient was 0.770, 0.811, 0.710 and 0.942 respectively. ~~Figure 4 shows the correlation for the right kidney at 1-year follow-up.~~ For a small number of kidneys (~5%) differences greater than 30% between

automated and semiautomatic methods were observed. Methods are being tested to improve robustness and automatically detect these outliers.

Table 2 describes the ability of the automated technique to ~~reliably~~ detect a decrease in renal volume for patients with occluded renal arteries when preoperative imaging is compared with the moment of detecting renal occlusion.

Discussion

In this study we demonstrate the accuracy of fusion-based software to automatically detect and calculate renal volume changes during follow-up after aortic endovascular repair. Using the established, reproducible, semi-automated technique to calculate renal volume (9), we have calculated renal volume in a sample of 16 patients. Using a process involving fusion techniques, we were able to assess the automated detection of renal volume and calculation of volume changes in CT images gained throughout the surveillance period. In addition comparing patients with and without any renal changes, the automated detection accurately ascertained the presence of renal volume both with and without contrast, and identified renal artery occlusion accurately. We believe this new technique may provide a robust, timely and reliable method for advanced analysis of postoperative surveillance studies; thereby a more accurate assessment can be performed in routine practice outside of investigational protocols.

As shown in different studies, renal volume is a reproducible and valid marker of renal impairment when decreased blood supply or anatomic causes for renal impairment are present. Renal volume has been assessed in various urologic studies as a predictor of graft function in living donor transplantation (12)(13). Furthermore, other urologic studies have observed a strong correlation between renal volume,

calculated with enhanced and unnonenhanced CT, and renal function estimated with nuclear medicine renal scans (14). This methodology to assess the renal volume is a complex and resource-intensive procedure which requires expensive and complex software, an extensive learning curve, and time. These characteristics may render it impractical for use in a busy daily practice outside of investigational applications, and inaccessible in many resource-limited environments. The precision of the method used for renal volume assessment in this manuscript has been evaluated applying the equation developed by Isotani et al(15) et Shomiyama et al(10). These authors developed an equation to predict postoperative renal function after nephrectomy by renal volume change and they found a correlation between predicted and observed eGFR of 0.83. Applying this equation, our correlation between predicted and observed eGFR was 0.844, (p< 0.000), a result comparable with the already published literature. Thus, we believe that this process may produce a functional method to detect changes in kidney volume, which, if automated, could provide a predictive and automatic notification regarding renal malperfusion to clinicians who are mandated to survey patients following aortic aneurysm repair.

The relationship between vascular clinicians and advanced imaging has been evolving over three decades. Isovoxel imaging and post processing software has made 3D manipulation of anatomic images possible, and facilitated the use of complex endovascular stent grafts for the repair of thoracoabdominal and juxtarenal aneurysms. Advanced imaging techniques such as 3D fusion have been recently introduced to operative procedures the advent of hybrid operating theatres and fixed imaging systems capable of performing cone-beam CT scans in the operative

environment. Use of advanced imaging has changed practice where available, because it has been demonstrated to reduce radiation exposure and contrast utilization in both EVAR and complex endovascular procedures (16)(17)(18). The potential postoperative applications remain unexplored in either hardware or software based systems. With the aim of extending fusion techniques during follow-up, we have tested the accuracy of a fusion-based software to automatically calculate renal volume during follow-up. Compared to the previously-tested semi-automated process, the percentage of decrease in renal volume detected by the automatic fusion-based software is reliable with an ICC of 0.877 ($p= 0.001$) at one year of follow-up for the left kidney and 0.966 ($p<0.001$) for the right kidney. These data validate fusion-based software as a reliable tool to automatically measure renal volume. In addition, in the vast majority of our cases with renal occlusion the fusion-based automatic software detected at least at 25% decrease in renal volume on the CT scan at moment of detection when compared with the preoperative ~~one~~.

If a study of renal event rate in the published literature were understaken, it would be observed that renal artery angulation should play some role in the discussion of renal volume loss. Renal artery angulation has been assessed in different studies to determine their impact and correlation with renal function during follow-up (19) and is hypothesized to be the cause of renal impairment after aneurysm repair. However, despite careful analysis, even observed changes of renal artery angulation after implantation of fenestrated and branched devices (4) have not been reliably associated with renal impairment~~, and are challenging to reproduce~~. The same results have been published by Ou et al. (6), finding no relation between postoperative renal impairment and the changes in the stent and vessel orientation, even if all the patients suffering

stent deformation presented renal impairment. This failure of correlation even remains true when ~~haemodynamic~~hemodynamic outcomes are improved with caudal orientation of renal stents(20). Thus, despite much suspicion that forced anatomic changes may bear some culpability for the deterioration of renal function often seen after aneurysm repair, contemporary imaging techniques have failed to provide proof. We believe a functional indicator, such as renal volume, which links anatomic change to important perfusion-related outcomes provides a surrogate measure of stent performance, and may be a better indicator of the 4-dimensional behavior of the stents. If automated, this could become a powerful and useful tool for clinicians who have a busy aneurysm practice. Furthermore, the ability to detect ~~chance~~ using an imaging technique that does not involve contrast makes it more practical for use in patients who have low grade renal impairment from any cause.

This study is a retrospective, pilot study to test the feasibility and accuracy of this technique and thus included only a limited number of patients. Another limitation can be consider the reproducibility of the semi-automated method, but it has been tested applying the formula developed by Isotani et al(15) . Furthermore, the impact of asymmetric changes in renal volume, as in the scenario where one of two accessories renal arteries is embolized has not been fully assessed. More work is needed to make this process fully automated and applicable to imaging processing platforms in all jurisdictions.

Conclusion

This is the first report of a fusion-based algorithm to detect changes in renal volume during postoperative surveillance using an automated process. Using this technique,

the standardised assessment of renal volume could be implemented with greater ease and reproducibility in the current follow-up of endovascular procedures. Renal volume has demonstrated to be a reliable marker of renal impairment.

Conflict of Interest Disclosure: TM Mastracci Research/Educational Support from Cydar Medical; Consulting of Cook Medical. G Penney Co-funder/Employee of Cydar Medical.

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FIGURES LEGENDS

Figure 1. Renal volume calculated with the semiautomated software. **a.** 3D VR reconstruction of the kidney selected. **b.** MPR view of the kidney selection. **c.** Renal contour in an axial view. **d.** Estimation renal volume

Figure 2. Renal volume calculated with the new fusion-based automatic software. **a.** Manually ~~selection~~ points in the preoperative CT **b.** Manually ~~pick~~ kidney centre in the postoperative CT scan. The kidneys are then represented in orthogonal views on post processing software so their three dimensional volume can be assessed **c.** Preoperative kidney volume. **d**. Postoperative kidney positioned and scaled, needing to be enlarged by 81% to accurately fuse with preoperative kidney

Figure 3. Correlation between predicted eGFR, based on renal volume calculated with the semiautomated process, and observed eGFR

~~**Figure 4.** Correlation between the semiautomated process and the new fusion-based automatic software for the right kidney at 1-year follow-up~~

Demographic characteristics	Non occlusion group	Occlusion group
Age at procedure (years) (median, range)	70.50 [65.25-81.50]	71.50 [65.25-78.25]
BMI (kg/m^2) (median, range)	29.8 [22.6-35.1]	22.8 [21.5-26.3]
Sex (%)		
Male	87.5 (n=7)	87.5 (n=7)
Female	12.5 (n=1)	12.5 (n=1)
Hypertension (%)	75 (n=6)	83.3 (n=5)
Dyslipidaemia (%)	75 (n=6)	100 (n=6)
COPD (%)	50 (n=4)	100 (n=6)
Smoking (%)		
Yes	0 (n=0)	33.3 (n=2)
No	25 (n=2)	50 (n=3)
Former	75 (n=6)	16.7 (n=1)
Diabetes (%)	25 (n=2)	16.7 (n=1)
Ischaemic heart disease (%)	62.5 (n=5)	50 (n=3)
Chronic kidney disease (eGFR<60 ml/min) (%)	25 (n=2)	66.7 (n=4)
Aneurysm size (mm) (median, range)	61 [56-72]	68 [61-75]
Preoperative renal function (ml/min) (median, range)	80.5 [49.25-89.75]	55 [42.25-74.50]

BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; eGFR: estimated Glomerular Filtration Rate

Table 1. Demographic characteristics divided by groups.

Patient number	Renal artery occluded	Time occlusion	% Decrease renal volume
1	Left	1 year follow up	61
2	Left	1 month follow up	29
3	Left	1 year follow up	16
4	Left	1 month follow up	13
5	Right	1 year follow up	49
	Left	1 year follow up	23
6	Right	1 month follow up	35
7	Right	1 year follow up	74
8	Left	1 month follow up	19

Table 2. % Decrease in renal volume detected by the automatic method at the moment of renal artery occlusion.

Figure 1A

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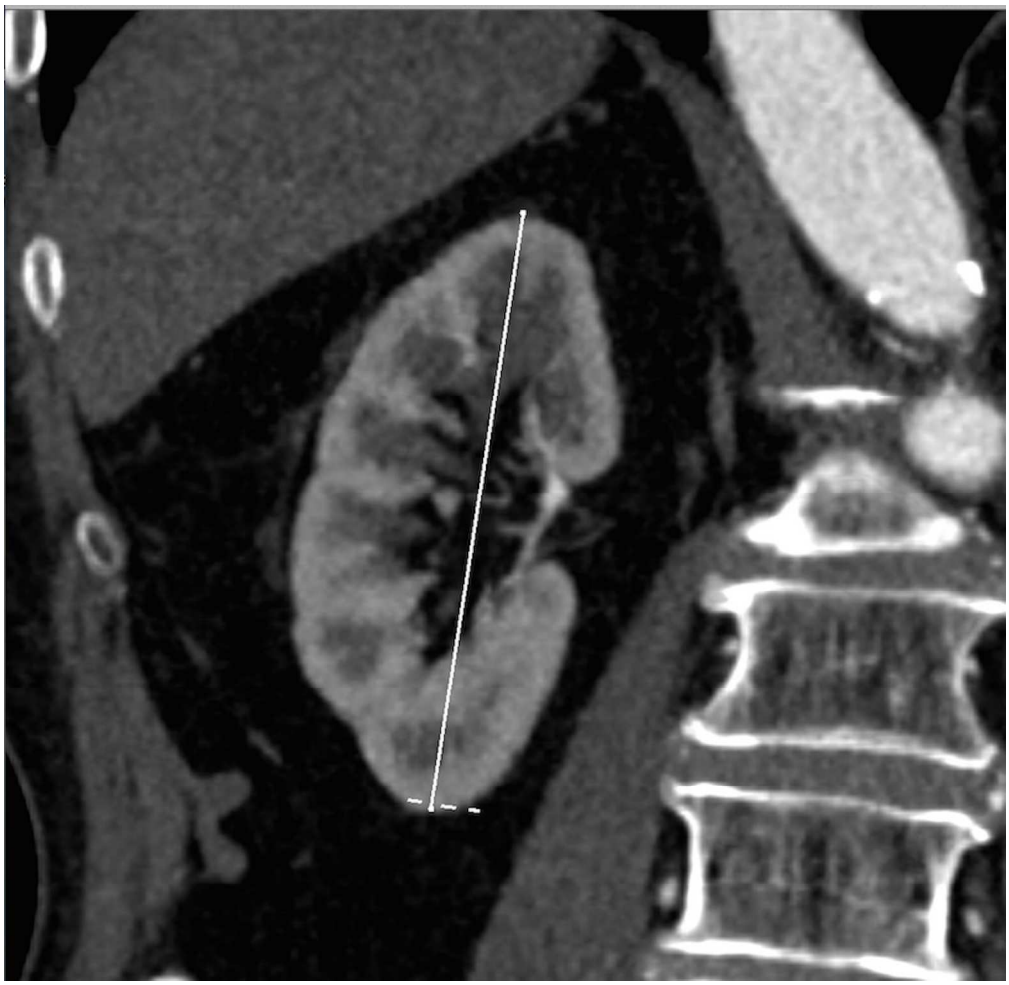

Figure 1B

286x278mm (300 x 300 DPI)

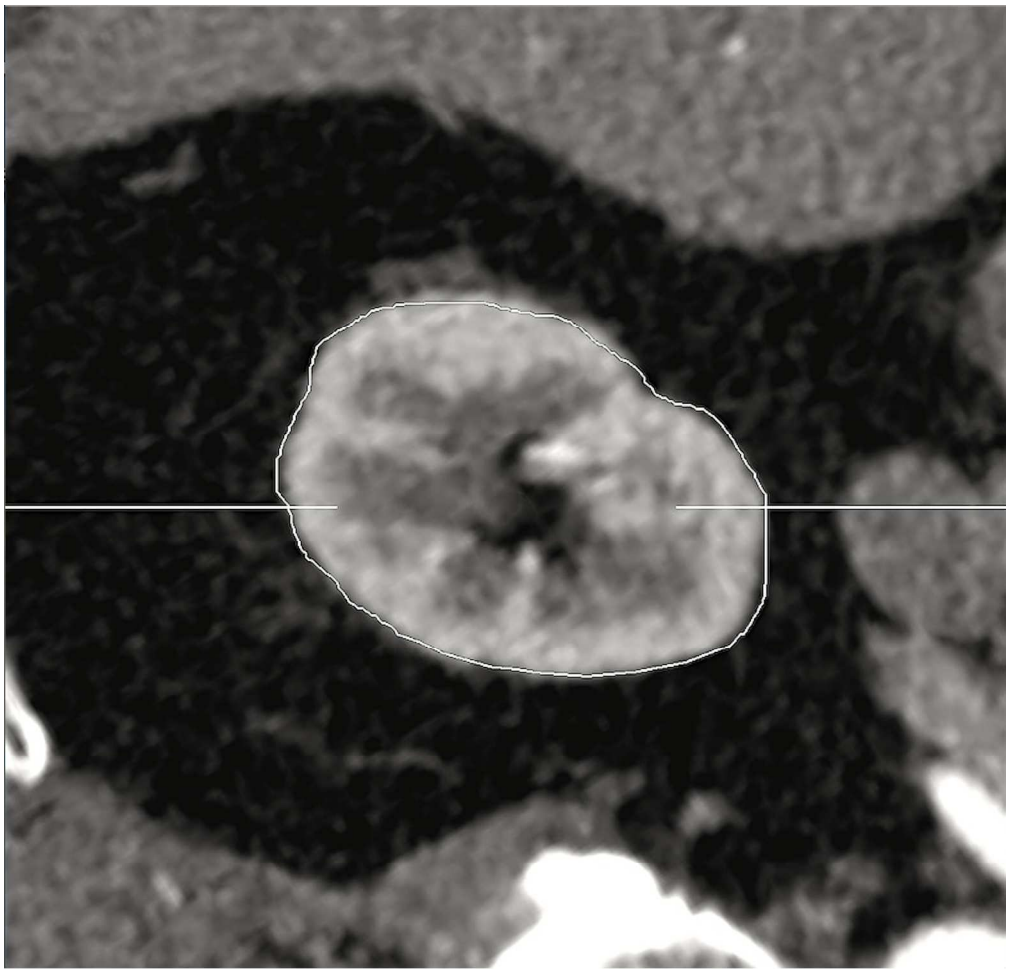

Figure 1C

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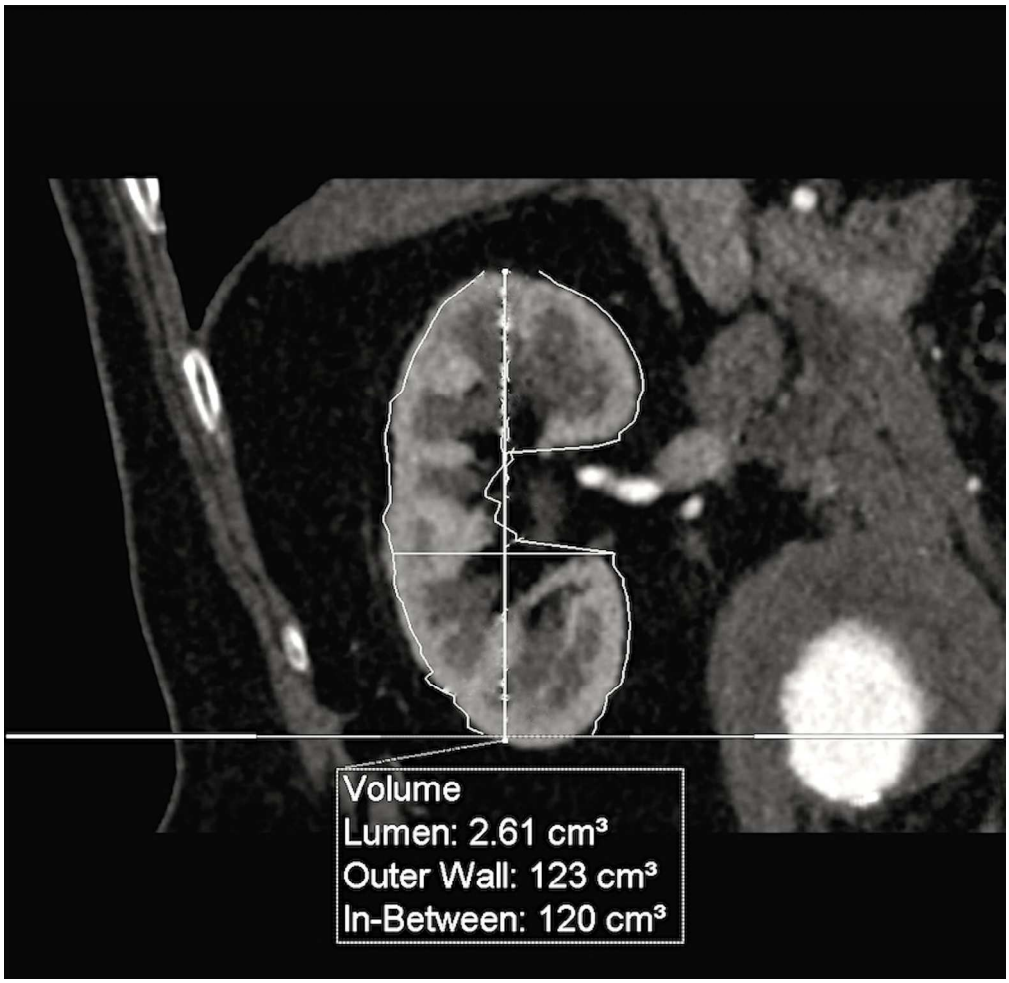

Figure 1D

284x276mm (300 x 300 DPI)

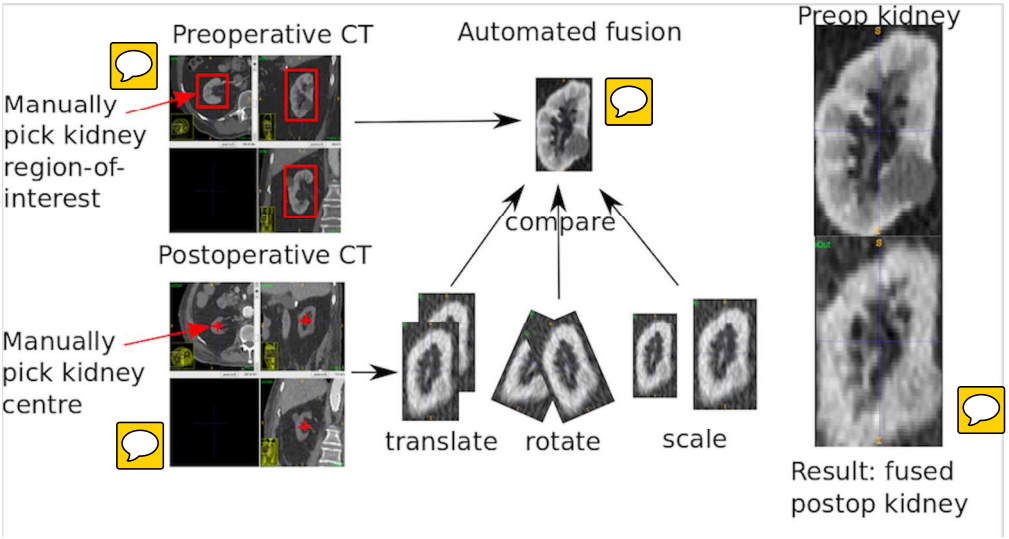

Figure 2

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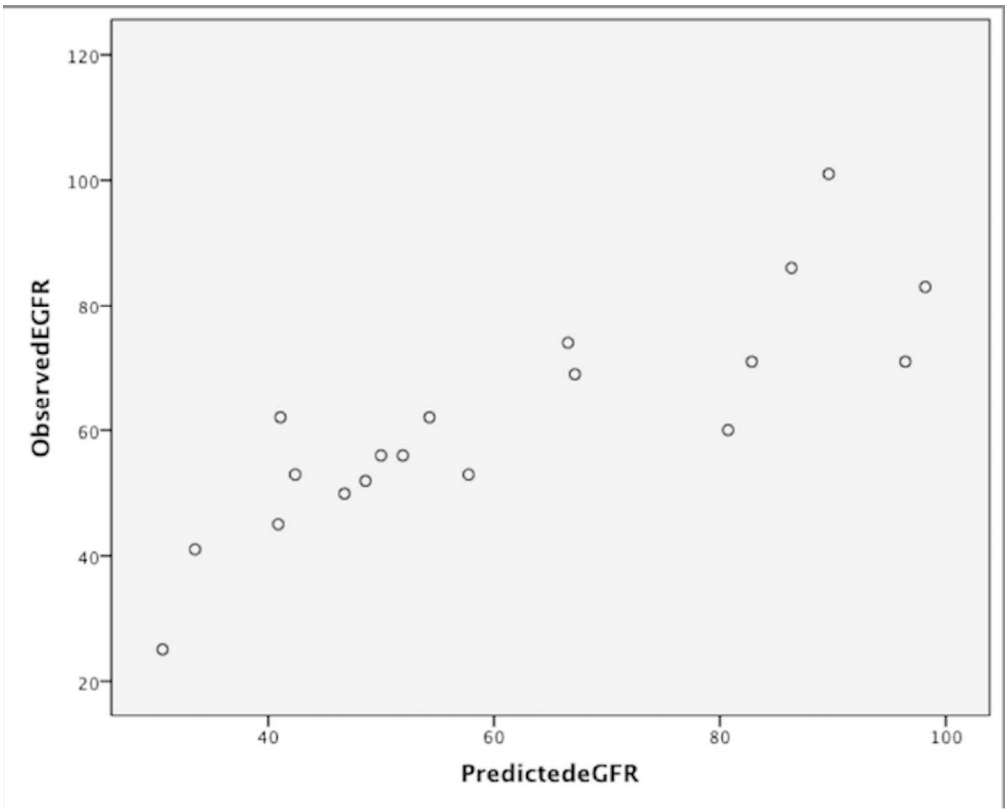

Figure 3

218x175mm (300 x 300 DPI)