3D Reconstruction of Wilms' Tumor and Kidneys in Children: Feasibility and Usefulness

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Abstract

Introduction: Wilms' tumor (WT), or nephroblastoma, is the most common type of malignant kidney tumor in children. The surgical phase is a key stage in WT management. The main objective of this study was to determine the feasibility of WT segmentation and 3D reconstruction. The secondary objective was to assess the usefulness of these 3D reconstructions in the surgical planning phase and in the selection of patients for nephron-sparing surgery.

Materials and Methods: 14 scans from 12 patients were manually or semi-automatically segmented by 2 teams using 3D Slicer software. 3D reconstructions were then generated from the segmented images. Inter-individual variability was measured based on the Dice index. The pre-chemotherapy scan (at diagnosis) and the post-chemotherapy scan (before surgery) were segmented for 2 patients in order to measure the tumor volume reduction. The utility of 3D reconstructions for the surgical planning phase was evaluated by 4 pediatric surgeons using a 5-point Likert scale. The possibility of undertaking nephron-sparing surgery was evaluated according to the criteria defined in the UMBRELLA SIOP-RTSG 2016 protocol.

Results: Segmentation of the renal tumor, healthy kidney, pathological kidney, arterial and venous vascularization could be performed for all of the patients in this study. Urinary cavities segmentation could only be performed for 5 out of 14 scans that had a delayed acquisition phase. The mean time required to carry out these segmentations was 8.6 hours [3-15 hours]. The mean Dice index for all of the scans was 0.87 [0.83-0.91]. The mean Dice indices for each anatomical structure were 0.95 [0.91-0.97] for the renal tumor, 0.87 [0.69-0.96] for the pathological kidney, 0.95 [0.93-0.96] for the healthy kidney, 0.84 [0.74-0.91] for the arterial vascularization, and 0.77 [0.58-0.86] for the venous vascularization. All the surgeons who were interviewed agreed that the 3D reconstructions were realistic representations and useful for the surgical planning phase. The images reconstructed in 3D allowed most of the criteria defined by the Umbrella SIOP-RTSG 2016 protocol to be evaluated regarding the selection of patients who could benefit from a conservative surgery.

Conclusion: Three-dimensional representation appears to assist surgeons with the surgical planning phase by allowing them to better anticipate the operative risks. 3D reconstructions can also be an additional tool to better select patients for nephron-sparing surgery. However, the manual or semi-automatic method used is very time-consuming, making it difficult for a routinely use. Developing techniques to automate this segmentation process, therefore, appears to be essential if surgeons and radiologists are to use it in daily practice.

Keywords: Wilms' tumor, segmentation, 3D reconstruction, surgical planning, nephron-sparing surgery

Introduction

Wilms' tumor (WT), or nephroblastoma, is the most common type of malignant kidney tumor in children, affecting 1 in 10,000 children *(1,2)*. Its peak incidence occurs between 2 and 5 years of age, with 95% of diagnoses being made before 10 years of age *(3)*. WT develops from the cortex or the medulla, which can then invade the urinary cavities and, in 6% of cases, the tumor can invade the renal vein and the inferior vena cava as a thrombus *(3)*. Therapeutic management of this tumor varies depending on the recommendations of learned societies, notably the SIOP (Société Internationale d'Oncologie Pédiatrique) in Europe and the COG (Children's Oncology Group) in North America. Irrespective of the protocol followed, the surgical procedure remains a fundamental component of the management of these tumors, as the final prognosis is dependent on its successful implementation.

Total uretero-nephrectomy is the recommended surgical procedure for unilateral WT that occur in a non-syndromic setting. A nephron-sparing surgery (NSS) can be undertaken in specific cases, namely bilateral WT, single-kidney WT, WT occurring in a context of genetic predisposition to tumors, and in a syndromic context where there is an increased risk of renal failure (such as Denys-Drash syndrome or WAGR syndrome). In light of the good prognosis with this type of tumor, there is ample merit in decreasing treatment-related morbidity without increasing the risk of local or remote tumor recurrence *(1–4)*. In line with this notion of therapeutic de-escalation, carrying out conservative surgery is considered to be appropriate in certain well-selected cases of unilateral tumors. The SIOP has, therefore, defined criteria in order to select the patients most likely to benefit from NSS *(Umbrella protocol, SIOP-RTSG 2016, version 1 2018-A02878-47, 27/11/2018)*.

Concomitant with these developments, medical image processing techniques have also benefited from significant advances in recent years. Segmentation of anatomical structures on 2D images combined with 3D reconstruction allows the three-dimensional surgical field to be recreated. Such 3D reconstruction could greatly assist surgeons in the surgical planning phase with regard to anticipation of the preoperative risks and especially the vascular risks. Additionally, these 3D models could be an aid in surgical decisions by assisting with the selection of patients who are likely to be able to benefit from reconstructive surgery.

The primary objective of this work was to determine the feasibility of segmentation and 3D reconstruction of a specific type of pediatric kidney tumor. The secondary objectives were to assess its usefulness in the surgical planning phase and in the selection of patients for NSS.

Materials and Methods

We retrospectively selected 12 patients treated for nephroblastoma at our center between 2005 and 2018. Patients whose imaging was performed in another center or whose images were of low quality were excluded from this study. The CT-scan of these patients were downloaded from the Picture Archiving and Communication System (PACS) in DICOM (Digital Imaging and Communications in Medicine) format. These scans were anonymized using PACS anonymization software. For each scan, we selected a vascular acquisition phase and a delayed acquisition phase (when available). In total, 14 scans were selected for this study. The pre-chemotherapy scan (at diagnosis) and the post-chemotherapy scan (before surgery) were segmented for 2 patients in order to measure tumor volume reduction induced by chemotherapy.

The segmentation process (assigning a pixel to a region) was performed for each scan by 2 operators (a pediatric surgeon and a pediatric radiologist) to calculate inter-individual variability. For each CT scan, the different structures were segmented manually or semi-automatically, section by section: the Wilms' tumor, the pathological kidney, the healthy kidney, the arterial vascularization (aorta, renal arteries, superior mesenteric artery), the venous vascularization (inferior vena cava, renal veins), and the urinary tract (when a delayed acquisition phase was available).

The segmentation and 3D reconstruction process was carried out with 3D Slicer software version 4.8.1 (https://www.slicer.org/). This is an open-source software, used primarily for medical image processing. The various structures of interest were segmented manually (by a contouring method) or semi-automatically (using a thresholding method). Each structure was assigned a label (*Figure 1*). The 3D reconstruction of the various anatomical structures was then implemented using the "*merge and build*" module of 3D Slicer (triangular mesh method). Finally, a smoothing filter was applied to the 3D reconstruction (*Figure 2*). The time required to complete this 3D reconstruction and segmentation process was recorded for each scan.

The Dice similarity index was used to calculate the inter-individual variability of the reconstructions performed by the two operators.

Using X as the segmentation performed by operator 1 and Y the segmentation performed by operator 2:

Dice similarity index = $\frac{2|X \cap Y|}{|X \cup Y|} = \frac{2A}{2A+B+C}$

where:

A is the number of pixels present in class X and in class Y

B is the number of pixels present in class Y and absent in class X

C is the number of pixels present in class X and absent in class Y

The utility of 3D reconstructions for the surgical planning was evaluated by four pediatric surgeons (three senior surgeons and 1 junior surgeon) using a 5-point Likert scale. Three questions were asked:

- Are the 3D reconstructions realistic representations?
- Are 3D reconstructions useful for the surgical planning?
- Are 3D reconstructions useful for evaluating the possibility of performing nephron-sparing surgery?

To assess the possibility of performing NSS, the criteria defined in the Umbrella protocol *(SIOP RTSG 2016 Umbrella)* were evaluated on the 3D reconstructions; namely:

- Tumor restricted to one pole of the kidney or peripheral at mid-kidney
- Volume < 300 ml at diagnosis
- No preoperative rupture
- No intraluminal tumor on preoperative imaging in the renal pelvis

- No invasion of the surrounding organs
- No thrombus in the renal vein or the vena cava
- No multifocal tumor
- Excision can be performed with oncological safe margins
- The kidney remnant is expected to have a degree of remaining function
- At least 66% of the renal tissue should be spared after the tumor resection with a margin of healthy tissue, to provide sufficient protection against hyperperfusion. If this is in doubt, preoperative DMSA may be able to define the expected postoperative function.

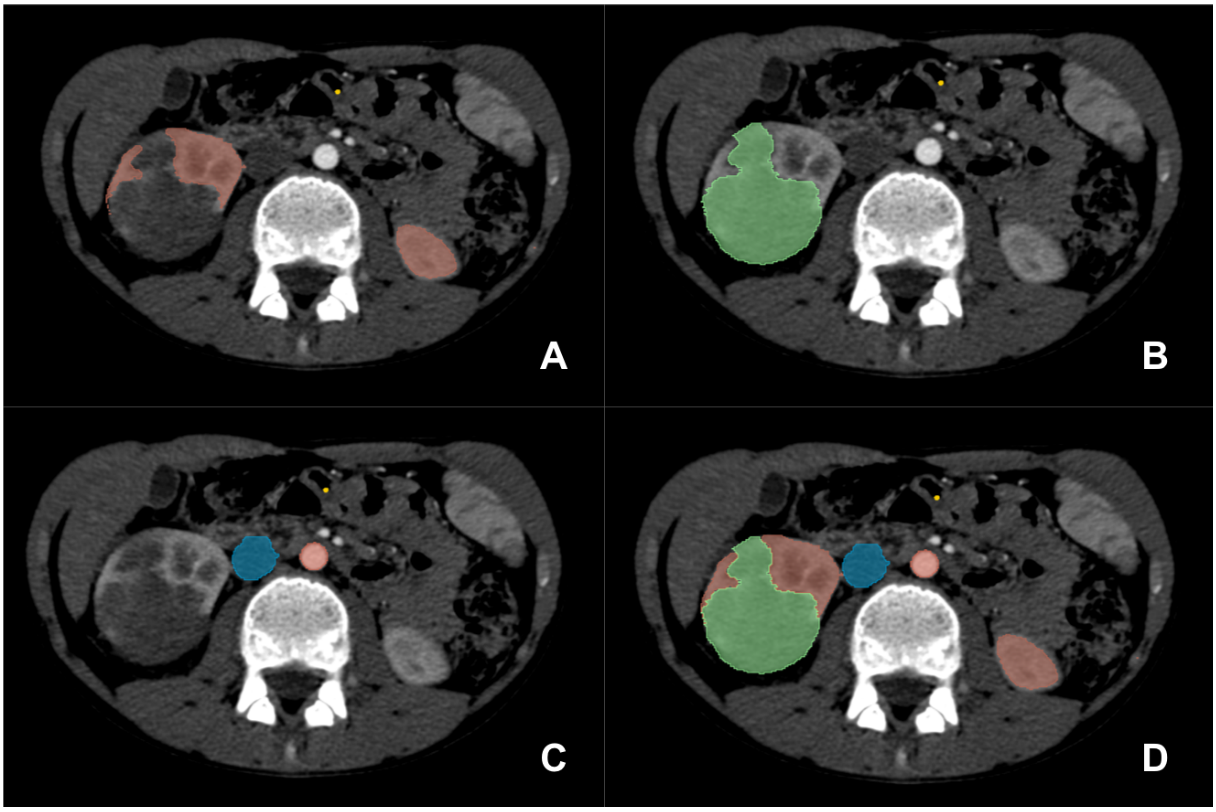

Figure 1: Segmentation of kidneys (A) and vessels (C) using a thresholding method. Segmentation of the renal tumor (B) using a contouring method. A merge of the different segmentations (D).

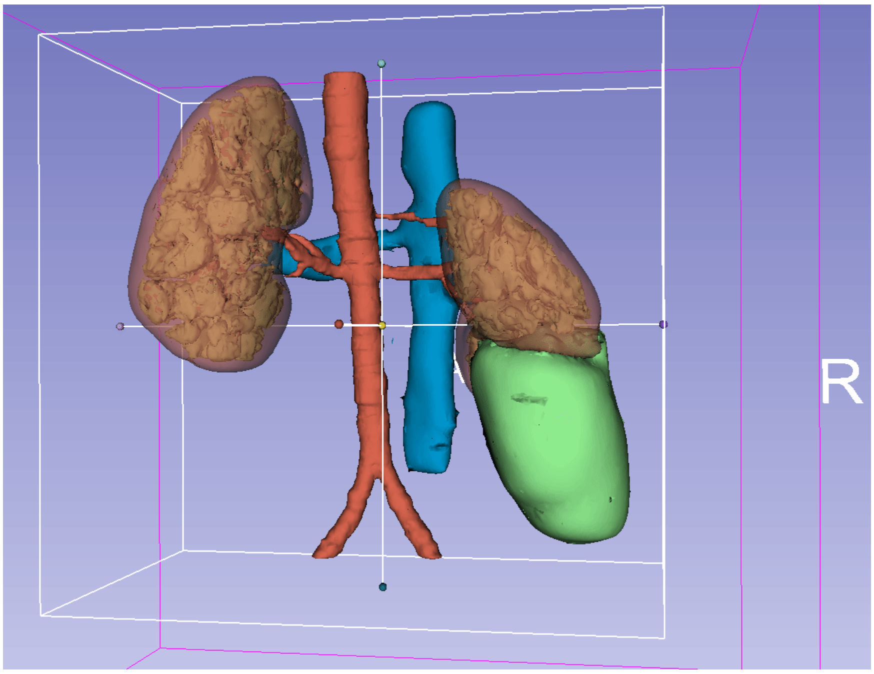

Figure 2: 3D reconstruction of kidneys (brown), Wilms' tumor (green), and their vascularization (arteries in red and veins in blue) with 3D Slicer software (version 4.8.1).

Results

Fourteen scans from 12 patients were selected. For 2 patients (patients 2 and 12), the 3D reconstruction was performed on 2 scans that had been performed at 1-month intervals (before chemotherapy and after 4 chemotherapy cycles), thereby allowing measurement of the reduction in tumor volume and thus the effectiveness of the chemotherapy. All 14 scans studied had a vascular acquisition phase but only 5 had a delayed acquisition phase that allowed segmentation of the urinary cavities.

Of these 12 patients, 5 were boys and 7 were girls, with a mean age at diagnosis of 67 months [13-179 months].

Feasibility

Segmentation of the WT, the kidneys, and the arterial and venous vascularization could be performed for all of the patients (*Figure 3*). Urinary cavities segmentation could only be performed for 5 scans with a delayed acquisition phase (*Figure 4)*.

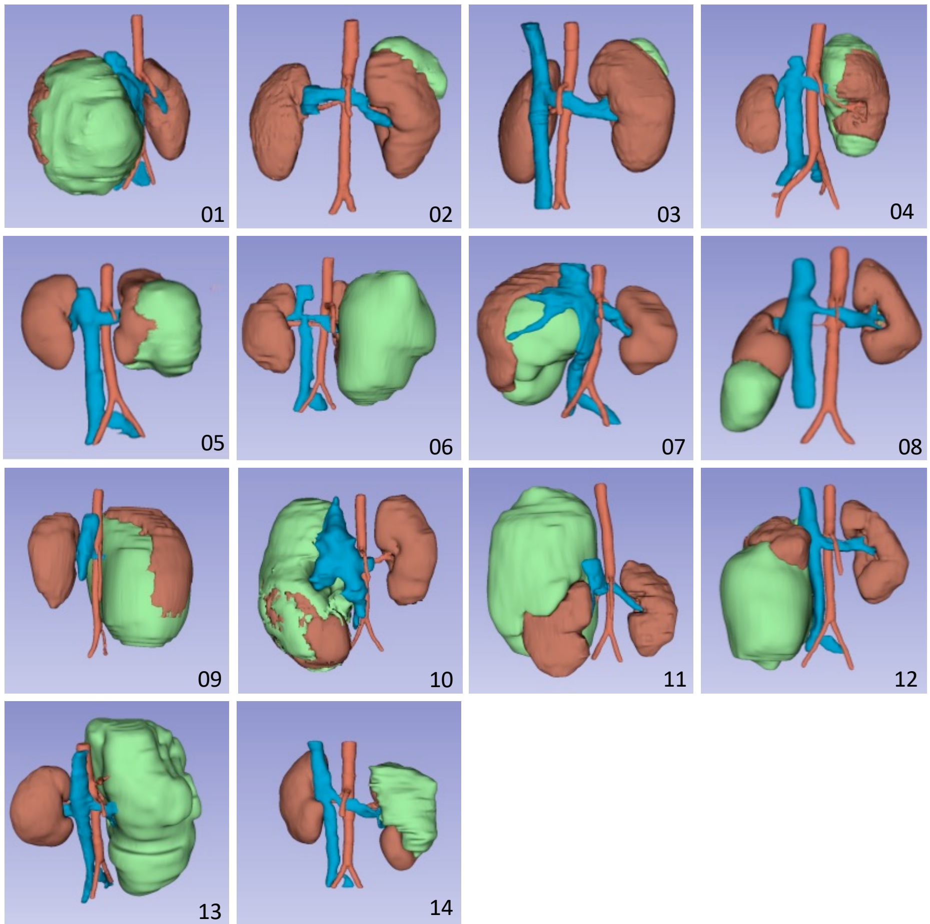

Figure 3: 3D reconstruction of the 14 scans: Wilms' tumor (green), renal parenchyma (brown), arterial vascularization (red), and venous vascularization (blue).

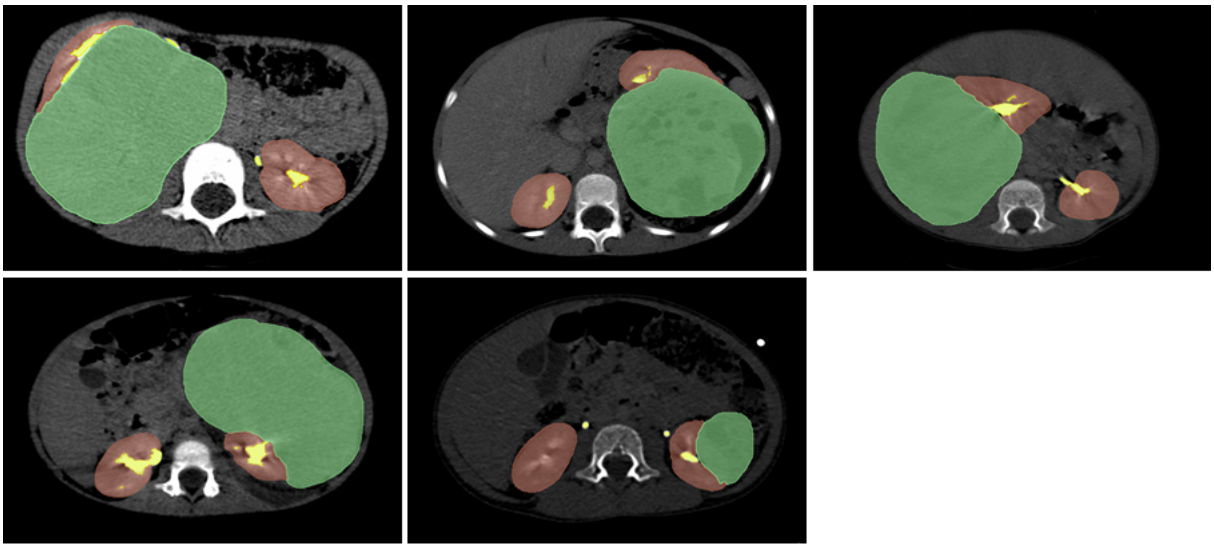

Figure 4: Segmentation of kidneys (brown), urinary cavities (yellow), and Wilms' tumor (green) for delayed acquisition phase scans.

Segmentation and 3D reconstruction time

The time required to complete these manual segmentations was recorded for each scan. The mean time was 8.6 hours [3-15 hours].

Inter-individual variability

The segmentations carried out by the two operators were compared using the Dice similarity index. The mean Dice index for all of the scans was 0.87 [0.83-0.91]. The mean Dice indices calculated for each of the anatomical structures were as follows: 0.95 [0.91-0.97] for the Wilms' tumor, 0.87 [0.69-0.96] for the pathological kidney, 0.95 [0.93-0.96] for the healthy kidney, 0.84 [0.74-0.91] for the arterial vascularization, and 0.77 [0.58-0.86] for the venous vascularization. The results are shown in Table 1.

Patients	Wilms' Tumor	Pathological Kidney	Healthy Kidney	Arteries	Veins	Average
1	0.94	0.83	0.96	0.87	0.75	**0.87**
2	0.91	0.96	0.94	0.82	0.70	**0.87**
3	0.95	0.92	0.95	0.91	0.58	**0.86**
4	0.92	0.88	0.94	0.89	0.77	**0.88**
5	0.96	0.89	0.96	0.84	0.69	**0.87**
6	0.96	0.82	0.93	0.83	0.84	**0.88**
7	0.94	0.92	0.96	0.85	0.86	**0.91**
8	0.97	0.79	0.94	0.82	0.72	**0.85**
9	0.95	0.69	0.95	0.74	0.82	**0.83**
10	0.96	0.92	0.94	0.81	0.79	**0.88**
11	0.96	0.88	0.95	0.82	0.84	**0.89**
12	0.95	0.88	0.95	0.83	0.83	**0.88**
Average	**0.95**	**0.87**	**0.95**	**0.84**	**0.77**	**0.87**

Table 1: The Dice similarity indices according to the anatomical structure for each patient

Evaluation of response to chemotherapy (tumor volume reduction)

For two of the patients, the tumor volume was measured before and after chemotherapy. The tumor volume decreased by 88% in the 1^{st} patient and by 93.3% in the 2^{nd} patient. The results are shown in Table 2 and Figure 5.

Patients	Tumor volume (cm^3)		Tumor volume reduction [%]
	Before CT	After CT	
2	25	3	**88**
12	885	59	**93.3**

Table 2: The response to chemotherapy (CT) based on calculation of the tumor volume before and after chemotherapy.

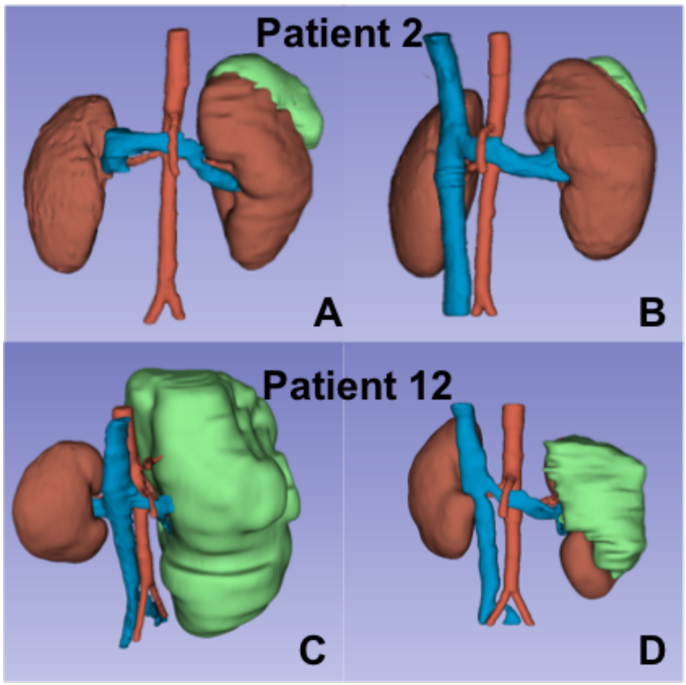

Figure 5: 3D reconstruction of the scans for patients 2 and 12 before (A and C) and after (B and D) chemotherapy.

Usefulness of 3D reconstructions for the surgical planning

All of the interviewed surgeons fully agreed or largely agreed that the 3D reconstructions were realistic representations of the reality and that they were useful for the surgical planning.

Three of the four surgeons thought that the 3D reconstructions were useful to evaluate the possibility of performing NSS. One surgeon thought that the 3D reconstructions did not always provide additional information about the possibility of performing NSS compared to 2D scan images.

Usefulness of 3D reconstructions for the selection of patients for NSS

The reconstructed 3D images allowed most of the criteria defined by the Umbrella Protocol *(SIOP RTSG 2016 Umbrella)* to be evaluated regarding the selection of patients who are likely to be able to benefit from conservative surgery. The last criterion, which requires functional imaging (a DMSA renal scan), could not be met. These 3D reconstructions were of particular relevance for the following criteria: the tumor location, a volume less than 300 ml at diagnosis, the relationship with the urinary cavities, the relationship with nearby organs, and the possibility of removal with adequate resection margins.

Discussion

WT is one of pediatric oncology's greatest success stories, with dramatic improvement in the prognosis as a result of advances in oncology management (chemotherapy, radiation therapy) and surgery *(2,4)*. Indeed, the 5-year survival rate for patients treated for WT has increased from 30% a few decades ago to almost 90% (at all stages combined) at present *(3)*. This extraordinary improvement in survival rates was achieved thanks to the studies and clinical trials carried out over the years by large multi-institutional organizations, including the SIOP (Société Internationale d'Oncologie Pédiatrique) in Europe and the COG (Children's Oncology Group) in North America *(3)*. Currently, long-term survival exceeds 90% for localized WT (Stage I to III) and it is greater than 70% for metastatic WT (Stage IV) *(1)*.

Surgery, chemotherapy, and radiotherapy are used to treat nephroblastomas. Their methods of use vary between countries, with a therapeutic strategy defined by the learned societies *(1)*. Irrespective of the protocol that is used, surgery continues to have a central role in the treatment of nephroblastoma as it allows resection of the primary tumor, thereby providing control of loco-regional (staging) and metastatic invasion.

The Contribution of 3D Reconstruction to Surgical Planning

Medical image processing techniques have evolved considerably in recent years. Segmentation is a process that assigns a label to a pixel, thereby delineating anatomical structures that are relative to each other. This is an essential step before undertaking three-dimensional reconstruction of these anatomical structures.

3D reconstruction of the tumor and its vascularization assists surgeons with the surgical planning phase. This preoperative visualization of the renal tumor in three dimensions makes it possible to anticipate the risks of surgery, especially vascular risks. In the absence of preoperative chemotherapy, when surgery is the first line of treatment, the tumor is most often of considerable size. This results in a change in the normal anatomical relationships as well as compression of vascular structures, especially venous structures (inferior vena cava, renal veins), which can make their identification difficult during the surgical procedure. 3D analysis of the kidney and its vascularization in the preoperative phase of the surgery could thus facilitate recognition of these structures when the surgical procedures are being carried out. Surgeons consider that analysis of a 3D model is more “natural” than analysis of the 2D CT (or MRI) images since it allows them to preview the operating field as they will see it when undertaking the surgical procedures.

The Contribution of 3D Reconstruction in the Selection of Patients for NSS

The very good prognosis with this tumor allows the morbidity of treatments to be reduced without increasing the oncological risk. One of the possible consequences of this pathology and its treatments is the development of end-stage renal failure (ESRD) in Wilms’ tumor survivors, which results in the patient requiring dialysis and/or renal transplantation *(5)*. The risk of ESRD is a particular concern in patients with bilateral WT (5-14% of patients), a single kidney WT, or a WT occurring in a syndromic context. For example, the risk of ESRD occurring after 20 years of follow-up is estimated to be 43.3% in patients with WAGR syndrome (Wilms’ tumor, Aniridia, Genitourinary malformations, and mental Retardation) and 82.7% in patients with Denys-Drash syndrome *(5,6)*. Conservative surgery (nephron-sparing surgery) is, therefore, recommended for these patients, whenever possible, in order to preserve the maximum amount of renal parenchyma and thus limit the risk of progression to ESRD.

The indication of conservative surgery is less clear for patients with unilateral WT in the absence of an exacerbating syndrome. The risk of progression to ESRD in these patients is extremely low, in the range of 0.7% at 20 years of age *(5,7)*. However, some series have reported a risk of renal damage in relation to a glomerular hyperfiltration phenomenon occurring after total nephrectomy *(5,7,8)*. It is essential to select the patients who can benefit from this conservative surgery, as otherwise the rate of local recurrence will increase. The SIOP has, therefore, issued recommendations *(SIOP RTSG 2016 Umbrella)* to accurately identify the patients with unilateral WT who can benefit from this conservative surgery.

3D reconstruction of renal tumor and kidneys can, therefore, be a valuable aid in the identification of these patients. 3D reconstruction also appears to be particularly useful for accurate calculation of the diagnostic tumor volume as well as the volume of the renal parenchyma that can be retained. Indeed, 3D reconstruction allows for more accurate calculation of the tumor volume than 2D imaging (whereby the tumor volume is usually estimated from 3 measurements taken in 3 orthogonal axes). This hypothesis has been confirmed by Durso *(9)*, who found that three-dimensional volume reconstructions were more precise than traditional 2D methods for estimating renal volumes and tumor volumes. He concluded that three-dimensional volume reconstructions are more accurate, reproducible, and more clinically useful in estimating volumes for urologists managing patients with renal tumors. Therefore, evaluation of a chemotherapy's effectiveness is more reliable when the tumor volume is calculated based on three-dimensional reconstruction.

Three-dimensional representation also appears to be more useful than 2D imaging to visualize a tumor's relationship with the intrarenal urinary cavities, provided that delayed acquisition scans are available.

The authors of the Umbrella protocol claim that, for bilateral WT, MRI appears to be the best choice for staging and assessment of the treatment response. If renal MR Angiography is not feasible, a CT scan with 3D reconstruction can be an option for the preoperative planning in order to visualize the vascular pedicles and to assess the feasibility of NSS.

The usefulness of 3D reconstruction has already been demonstrated in adults. For example, Wang *(10)* concluded that 3D visualization assists with the surgical planning phase for laparoscopic partial nephrectomies in complicated adult renal tumors. Chen *(11)* stated that 3D reconstructions are not only useful during the surgical planning phase but also during surgery, as they allow segmented models to be superimposed on the surgical field as part of augmented reality. Porpiglia *(12)*, in a review of the literature, confirmed that 3D technology (3D printing and 3D digital models) is not only useful for the surgical planning but also for teaching and training of doctors as well as to generate preoperative information that can be presented to the patient and their family.

Limitations/Constraints

This study identified the constraints and limitations for performing these three-dimensional reconstructions in daily practice. First, the scans of these patients were collected retrospectively. There was hence a degree of heterogeneity regarding the image quality with different image acquisition protocols. Some of the scans were of poor quality. This can be explained by the use of low-dose protocols in children to limit irradiation as well as by the low level of body fat in children that limits the contrast differences between anatomical structures on scans.

On the other hand, only 5 scans (out of 14) had a delayed acquisition phase that allowed 3D reconstruction of the urinary tract. It is, therefore, essential to standardize image acquisition protocols in order to obtain operable and good quality images, which is something that has been implemented in our center as a result of this study.

The main impediment to performing these routine segmentations and 3D reconstructions is the time it takes to complete them. Indeed, in our study, the average time to perform these segmentations and 3D reconstructions was 8.6 hours, using either a manual or semi-automatic method. Although the time required for segmentation tended to decrease the more the software was used, developing techniques to automate this segmentation process as much as possible appears to be paramount. To the best of our knowledge, there is presently no fully automated method for segmentation of renal tumor in children.

Finally, performing these segmentations manually (or semi-automatically) is subject to the risk of human error. Due to the aforementioned reason regarding the assessments' implementation, our segmentations were carried out by two operators. The inter-individual variability appears to be quite acceptable in our series, with a mean Dice index close to 90%. However, when analyzing the Dice index for specific anatomical structures, it was found to be less than 80% for the venous structures. This is due to the poor image quality and the choice of the vascular acquisition time used for the segmentation. Again, standardization of the CT-scan protocols and automation of the segmentation process should improve these results.

Overview

The future will likely entail reliance on MR images, as this non-irradiating imaging technique is increasingly used in this indication, provided that good quality images are available, which currently remains a challenge for children in this age group. The segmentation techniques used in this study with CT images (notably thresholding and contouring) can equally be used with MR images.

In order to reduce the time required to complete these three-dimensional reconstructions, our team is currently working on the use of artificial intelligence-based tools (case-based reasoning, deep learning) to automate the segmentation process *(13)*.

Standardization of image acquisition protocols is also essential in this context. This will make it possible to use images of homogeneous quality, as well as to have all the acquisition phases (especially delayed acquisition phase) to be able to more readily identify the different anatomical structures that are to be segmented (urinary tract, vessels). This standardization of protocols is a fundamental step to automation of the segmentation process.

Conclusion

Segmentation with 3D reconstruction of renal tumors, kidneys, and their vascularization in children is a feasible process that has several advantages. Indeed, three-dimensional representation assists surgeons with the surgical planning by allowing them to better anticipate the risks of the surgery, especially vascular risks. 3D reconstructions also appear to help when it comes to selecting patients for conservative surgery. However, the manual or semi-automatic method is very time-consuming, making routine use of such reconstruction difficult. The development of techniques to automate this segmentation process, therefore, appears to be essential if surgeons and radiologists are going to be able to use it in daily practice.

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