Appendix E1: Technical Guidelines for Imaging Neuroblastic Tumors

Technical Recommendations for CT Scanning

The use of multidetector computed tomography (CT) dramatically reduces the need for sedation, provided there is adequate immobilization of children. The use of oral contrast material, or water, to delineate the digestive tract is usually not required. Oral contrast agents are poorly tolerated in patients with cancer, and at multidetector CT, fast acquisition, thin sections, and multiplanar reconstructions enable excellent differentiation between the bowel and the tumor (64). A contrast enema is not required, even for pelvic tumors.

Nonenhanced CT series will define intratumoral calcifications, but these examinations are not mandatory and should be used only in doubtful cases and focused on the primary tumor volume. One contrast material–enhanced series is usually sufficient to assess the tumor extent. Well–tolerated low-osmolarity, nonionic) contrast agents should be used with iodine concentrations of 300–350 mgI/mL, with a total volume of 1.5–2.0 mL per kilogram of body weight. The perfusion rate should be adapted to the patient's age and the intravenous catheter line diameter to ensure appropriate enhancement and is usually between 0.8 and 2.0 mL/sec. The scanning delay should be adjusted to achieve both arterial and venous enhancement and depends on the patient's age, the anatomic region assessed, and the acquisition time. The CT acquisition is usually begun just after the end of the contrast agent injection for the neck and chest. To achieve both venous and portal phases during the same series, the scanning delay is longer abdominal and pelvic studies: between 35 and 60 seconds after the beginning of the injection, depending on the patient's age, the perfusion rate, and the acquisition time. Injection is preferably performed with an automatic injection device. An automatic bolus detection option can be used to adjust the scanning delay.

The beam collimation should be adjusted to the CT machine—specifically, the number of detector rows—but the nominal section thickness should be between 0.5–2.5 mm and the reconstruction thickness should be between 2 and 5 mm. The use of a minimal tube rotation time is recommended to reduce acquisition time. Recommended pitch values are between 1.0 and 1.5, providing a reasonable compromise between a short acquisition time and sufficient longitudinal spatial resolution (ie, in z–axis). The tube voltage and current should be adapted to the patient's age and weight and to the anatomic region studied. The tube voltage is usually set between 80 and 100 kVp for the trunk in newborns and infants and between 100 and 120 kVp in other situations. The tube current should be adjusted to obtain a final mean absorbed dose (ie, CT dose index volume) that is in agreement with the current pediatric recommendations or dose reference levels (65–70).

Technical Recommendations for MR Imaging

Since image quality is highly sensitive to motion artifacts, MR imaging should be performed in young children by using sedation or general anesthesia, with adapted monitoring. Various sedation protocols (71–74) may be used, depending on the local strategies. Safety rules include use of auditory protection and specific absorption rates below recommended levels, especially in infants and newborns.

MR imaging always involves customizing the imaging settings to the individual patient and the local MR unit. There currently is no consensus regarding the optimal MR protocol to use in patients with neuroblastoma. Appropriate compromises regarding the field of view, matrix, section thickness, signal–to–noise ratio, and acquisition time should be reached, with the acquisition time being optimized by using phased–array coils and parallel acquisition. Each protocol should be adapted to the available options—notably motion–reducing sequences and respiratory or cardiac gating.

The acquisition planes should always include the axial plane and at least one longitudinal plane (coronal or sagittal). A three–plane study is strongly recommended for paraspinal neuroblastosomas to assess foraminal and intraspinal extensions. The orientation of the coronal views should be adjusted on the sagittal view to yield images that demonstrate the full foraminal and intraspinal tumor extent on the same coronal image.

The field of view and matrix should be adjusted to the patient's size and anatomic regions. The in–plane pixel size should range between 0.5 arc mm, and the section thickness should be between 3 and 4 mm for two–dimensional imaging and between 1 and 2 mm for three–dimensional gradient–echo imaging to optimize the spatial resolution.

Appropriate MR sequences are spin–echo, fast spin–echo, inversion–recovery, and spoiled gradient–echo T1–weighted sequences, and fast spin– and short–tau inversion–recovery T2–weighted sequences. The tissue contrast on T2–weighted images can be increased with use of fat saturation or water–excitation options. The use of gadolinium–enhanced T1–weighted sequences is optional, but if these sequences are used, they should be performed with fat saturation to increase the contrast against fatty tissues. The use of gadolinium–based contrast material should be avoided in children with impaired renal function because of the risk of secondary nephrogenic systemic fibrosis (75).

CT and MR Angiography

Noninvasive angiography can be performed in children by using CT (multiphase acquisitions with bolus contrast agent injection and maximum intensity projection reconstruction) or MR imaging (with contrast–enhanced or nonenhanced methods) (76–78). To our knowledge, the possible benefit of using CT or MR angiography in patients with neuroblastoma has not been specifically addressed in the literature, and in our opinion, angiography is not required for staging or preoperative assessment.

The specific situation of a lower mediastinal tumor between the T9 and T12 spinal levels is associated with a theoretic risk of spinal cord ischemia caused by surgical injury to the anterior spinal (Adamkiewicz) artery. However, this risk is very low in children, and according to our group, preoperative angiography is not necessary. If angiography is required by the surgeon, it is possible to assess the anatomic level of the origin of the small artery with either CT angiography (79) or MR angiography (80,81), although these methods have not yet been evaluated in patients with neuroblastoma.

Tumor Measurements

We recommend that three–dimensional measurements of the primary tumor always be provided at the time of diagnosis and later during therapy observation. One–dimensional measurements have been proposed for tumor evaluation (according to Response Evaluation Criteria in Solid Tumors [RECIST] criteria) (82,83). However, because of the complex shape of pediatric tumors such as neuroblastosomas, the use of three–dimensional evaluation is considered more appropriate (84). Moreover, three–dimensional assessment yields a more realistic preoperative tumor volume measurement for surgeons and allows volume estimation. Measurements are easily obtained for well–circumscribed tumors. The largest transverse...
orthogonal diameters ($D_1$ and $D_2$) are obtained from the axial plane, and the height of the tumor ($D_3$) from one longitudinal (coronal or sagittal) plane is obtained either directly with MR imaging or with multiplanar reconstruction (Fig E1). The tumor volume ($V$) is obtained by using the class elliptical approximation: $V = D_1 \times D_2 \times D_3 \times 0.52$.

![Figure E1](image)

**Figure E1**: Three-dimensional measurements (arrows) of tumor volume obtained on contrast-enhanced (a) axial and (b) sagittal CT multiplanar reconstructions in 4-year-old girl with well-circumscribed prerenal ganglioneuroblastoma.

Measurements for complex-shaped masses or tumors associated with numerous adjacent lymph nodes are more difficult to obtain and less reproducible. In such situations, it is recommended that the whole tumor mass—that is, the primary tumor plus the adjacent lymph nodes—be measured in a single volume (Fig E2).

![Figure E2](image)

**Figure E2**: Whole tumor mass (primary tumor plus contiguous lymph nodes) measured in a single volume (arrows) on axial contrast-enhanced CT image in 4½-year-old boy with complex-shaped abdominopelvic neuroblastoma. Measurement is from the axial plane (height measurement not shown).

**IDRF Assessment**

To improve the recognition and description of IDRFs, it is recommended that various acquisition planes (with two-dimensional MR sequences) or multiplanar reconstructions (from 3D MR sequences or CT series) be used (Figs E3–E12). Relationships between the tumor and adjacent organs are best assessed by using acquisition planes perpendicular to the contact plane between the tumor and the adjacent structure. Relationships between tumors and vessels are best assessed with two planes—one in the long axis of the vessels and the other perpendicular to this axis—to assess the percentage of the vessel circumference surrounded by the tumor. A checklist of IDRFs is provided (Fig E13) to facilitate and ensure uniform and correct staging at diagnosis; however, this checklist is not intended to be a substitute for the local radiologist’s report.
**Figure E3:** Axial contrast-enhanced CT image in 3-year-old boy with left suprarenal neuroblastoma (*) shows the aorta, celiac artery (arrow), and splenic artery (arrowhead) separated from the tumor by a fatty layer. For these specific vessels, an IDRF is not present.

**Figure E4:** Nonenhanced (a) axial T1-weighted and (b) coronal T2-weighted MR images in 7-year-old boy with left mediastinal ganglioneuroblastoma. A "contact" is present between the tumor and the aorta—that is, less than 50% of the aorta’s circumference (arrow in a) is in contact with the tumor. This condition does not represent an IDRF. However, the anatomic location of the tumor—the costovertebral junction between the T9 and T12 spinal levels—is an IDRF because of the theoretic risk of spinal cord ischemia caused by surgical injury to the anterior spinal (Adamkiewicz) artery.
Figure E5: Axial T1–weighted MR image in 2½–year–old girl with right cervical ganglioneuroblastoma. A “contact” is present between the tumor (*) and the internal carotid artery (long arrow). The internal jugular vein (arrowhead) is “flattened” (ie, with reduced diameter but still partially visible lumen). For these vessels, an IDRF is not present. However, the compression of the airway (short arrows) in this patient should be considered an IDRF. If only the pharynx and the larynx, and not the trachea, are compressed, an IDRF should still be listed—as “other condition considered equivalent to the listed IDRF.”

Figure E6: Axial contrast–enhanced CT image in 2½–year–old boy with medial retroperitoneal neuroblastoma. The aorta (long arrow), both renal arteries (arrowheads), and right kidney (K) are completely encased by the tumor. The tumor infiltrates the duodenopancreatic block (short arrow). All of these structures, an IDRF is present.
Figure E7: Coronal contrast-enhanced CT image in 4-year-old boy with left retroperitoneal suprarenal neuroblastoma. The left kidney is displaced and distorted by the tumor (*) but not infiltrated, as the normal cortex (arrows) is still visible. This specific condition is not an IDRF. However, the involvement of the renal pedicle does constitute an IDRF.

Figure E8: Sagittal contrast-enhanced CT image in 4-year-old girl with right adrenal neuroblastoma. The liver (arrows) is distorted but not infiltrated by the tumor, but the left kidney is infiltrated by the tumor (as confirmed at pathologic analysis). The margins (arrowheads) between the tumor and the kidney are ill defined. This specific condition is an IDRF.
**Figure E9:** Axial nonenhanced T1-weighted MR image in 3-month-old girl with right mediastinal dumbbell neuroblastoma. The leptomeningeal cerebrospinal fluid spaces (arrowheads) are still visible, and the spinal cord signal intensity is normal. However, about one-half of the spinal canal in the axial plane is invaded (*), and the descending aorta (arrow) is partially encased. Both conditions are IDRFs.

**Figure E10:** Axial contrast-enhanced CT image in 5-year-old girl with retroperitoneal and pelvic neuroblastoma. The left iliac vessels (short arrow) are in contact with the tumor (not an IDRF), but the right iliac vessels (arrowheads) are completely encased (an IDRF). The tumor infiltrates the iliolumbar fossa (long arrows), a condition classified as “other conditions” and considered IDRF positive because of the risk of lumbar plexus surgery injury.
Figure E11: (a) Axial nonenhanced T1-weighted MR image (at L1-L2 spinal level), and (b) coronal and (c) sagittal T2-weighted images in 3½-year-old boy with right lumbar paraspinal neuroblastoma and foraminal and intraspinal extensions (dumbbell tumor). More than one-third (about 80%) of the spinal canal in the axial plane is invaded (long arrow in a and c, arrow in b), and the leptomeningeal spaces are not visible (an IDRF), but the spinal cord MR signal intensity is still normal. The right diaphragm crus is encased (an IDRF) (short arrow in a and c). The aorta (arrowhead in a) is in contact with the tumor (not an IDRF).
**Figure E12:** Axial contrast-enhanced CT image in 3-year-old girl with retroperitoneal neuroblastoma (arrows) infiltrating the mesentery (an IDRF). The mesenteric vessels are encased (an IDRF) (arrowhead).

**Figure E13 (PDF)**

**Imaging Data Storage**

All imaging data should be recorded and stored to allow retrospective reviews, either in a picture archiving and communication system or on CD-ROMs. The recommended format should be the most recent version of the internationally accepted Digital Imaging and Communications in Medicine (DICOM) format [http://medical.nema.org/].

**References**


