Neurofibromatosis Type I: Description of a Novel Diagnostic Scoring System in Pediatric Optic Nerve Glioma

Hadeel Eid1,2 Gabriel Crevier-Sorbo3 Ahmed Aldraihem1,4 Flavia Menegotto5 Nagwa Wilson1

Keywords: glioma, neurofibromatosis type 1, optic, pediatric, tortuosity

doi.org/10.2214/AJR.18.20044

Received April 23, 2018; accepted after revision October 4, 2018.

OBJECTIVE. Neurofibromatosis type 1 (NF1) is a multisystemic genetic disease in which patients develop benign tumors including optic nerve gliomas (ONG). Optic nerve thickening and tortuosity are radiologic markers of tumors but can also be present in children with NF1 who do not have gliomas, thus complicating screening and diagnosis. We undertook this study to retrospectively determine quantitative and qualitative diagnostic criteria using MRI of the orbits for ONG in children with NF1.

MATERIALS AND METHODS. MR images of the orbits obtained from 2003 to 2016 for children with and without NF1 were reviewed. Optic nerves were divided into three groups: NF1 with glioma (n = 71 nerves), NF1 without glioma (n = 151 nerves), and healthy control subjects (n = 66 nerves). The diameter of each nerve was measured at multiple locations. Two radiologists assessed tortuosity using validated criteria, and subarachnoid dilatation was quantified. Last, a composite score using both optic nerve diameter and tortuosity was proposed.

RESULTS. The mean diameter of the optic nerve was significantly larger in patients with NF1 with glioma compared with those with NF1 without glioma and with control subjects at all locations. Maximal nerve diameter greater than 2 SD above the mean maximal diameter for control nerves was considered abnormally enlarged. The tortuosity parameters were all significantly associated with ONG compared with absence of ONG in NF1. A scoring system derived from these data were highly reliable in differentiating ONG from absence of ONG in NF1.

CONCLUSION. The radiologic diagnosis of ONG in patients with NF1 is challenging. The scoring systems we describe provide a framework for simple radiologic criteria for ONG in these patients.

Neurofibromatosis type 1 (NF1), also known as Von Recklinghausen disease or peripheral neurofibromatosis, is a neurodermal dysplasia that was first described by Friedrich Daniel Von Recklinghausen in 1882 [1, 2]. The estimated frequency of this autosomal dominant disorder is 1 in 3500 live births, and half of patients have a family history of the disease [3]. The disorder likely stems from loss of function mutations of the NF1 tumor suppressor gene, which codes for a negative regulator of the RAS proto-oncogene called neurofibromin [4]. This change leads to overactivation of RAS and uncontrolled cell growth, putting patients at high risk of developing tumors throughout the CNS and in other tissues [5, 6]. The hallmark of the disease are neurofibromas, which are found in almost all patients. Plexiform neurofibromas, large tumors of peripheral nerves, are found in a third of patients [7]. The overall risk for brain tumors is five times higher in patients with NF1 than in the general population [8]. Tumors are usually World Health Organization (WHO) grade I, BRAF mutation–negative, pilocytic astrocytomas [9, 10]. Patients with NF1 are at risk of not only nervous system or neural crest-derived tumors but also tumors of the lung, thyroid, skin, breast, ovary, adrenals, and gastrointestinal tract as well as hematologic malignancies and sometimes rhabdomyosarcomas and neuroblastomas [7, 11–14].

Optic nerve gliomas (ONG) are the second most common tumor type in NF1, occurring in 15% of patients; bilateral ONGs are pathognomonic for NF1 [15–19]. ONGs can occur anywhere along the optic tract, and an anatomic classification was proposed by Dodge et al. [20] in 1958, defining tumors as involving the optic nerves alone (stage I); the chiasm with or without nerve involvement (stage II); or the hypothalamus, other adjacent structures, or both (stage III). Most of
Optic Nerve Glioma in Children With NF1

these tumors are asymptomatic WHO grade I pilocytic astrocytomas, but a subset of patients develop proptosis, progressive vision loss, and blindness [9, 21–23]. Early treatment of aggressive lesions can improve outcomes and suggests screening along with regular ophthalmologic examination is valuable in patients with NF1 whether or not they have symptoms of ONG [15].

The two main radiologic criteria used to characterize ONGs are thickening and tortuosity of the nerve [24, 25]. Previous studies have found that an optic nerve diameter greater than 3.9 mm can be used as a marker of glioma in patients with NF1 and that tortuosity is more common in those who go on to develop glioma [24–27]. Despite increasingly sophisticated MRI, differentiating between tortuosity and thickening of the optic nerve in patients with NF1 and in those with an ONG remains difficult. Through a retrospective analysis, we determined quantitative reference values for optic nerve enlargement and subarachnoid dilatation in patients with NF1 glioma and combined them with established optic nerve tortuosity parameters to create scoring criteria to diagnose anterior ONGs in patients with NF1.

Materials and Methods

Patient Population

This study was approved by the Research Ethics Board at the Montreal Children’s Hospital. MRI of the orbits performed at the Montreal Children’s Hospital between September 2003 and September 2016 for children with NF1 and children without NF1 who had radiographically normal optic nerves were identified. Only children younger than 18 years old at time of the imaging with available axial and coronal T2-weighted images of the orbits were included. Control participants were included only if they did not have a history of congenital or systemic disease, optic nerve hypoplasia, or optic neuritis or any signs of increased intracranial pressure. All patients with NF1 included in this study had contrast-enhanced axial and coronal T1-weighted images of the orbits were included. Control participants were included only if they did not have a history of congenital or systemic disease, optic nerve hypoplasia, or optic neuritis or any signs of increased intracranial pressure. All patients with NF1 included in this study had contrast-enhanced axial and coronal T1-weighted images of the orbits, although that was not a specific inclusion criterion.

Group Stratification

The optic nerves of patients with NF1 were divided into two groups: those in patients with clinically symptomatic ONG and those in patients without evidence of ONG. The MRI study at the first presentation of glioma was selected in the former group; for the latter, the first MRI study was selected.

Optic Nerve Diameter

A single reader who was blinded to any identifying information or clinical reports measured the diameter of each optic nerve. The diameter was measured at the thickest portions of the following locations: retroocular (< 10 mm from the posterior border of the globe), midsegment (> 10 mm from the posterior border of the globe), intracanalicular and prechiasmatic portions in the axial plane and retroocular, midsegment, prechiasmatic, and chiasmatic portions in the coronal plane. The chiasmic measurement in the coronal plane was defined for each optic nerve as the superoinferior length at the slice immediately anterior to the stalk (Fig. 1). For each group, the reader calculated the mean diameter at every location and in both planes as well as the mean maximal diameter of the individual nerves in each plane.

Optic Nerve Tortuosity

Armstrong et al. [27] described a 6-point scale for defining optic nerve tortuosity by MRI. The
scale was based on presence or absence of any of the following criteria in each optic nerve: interruption of the nerve out of the axial plane without return of the nerve segment, interruption of the nerve out of the axial plane with return of the nerve segment, deviation of the nerve within the axial plane either medially or laterally, increased curvature of the nerve when assessed in the sagittal plane, lack of congruity of the nerve border in more than one coronal section, and dilatation of the subarachnoid space (SAS) surrounding the optic nerve.

Using these criteria, two radiologists blinded to any identifying information or clinical reports independently assessed all MR images of the orbits for the presence or absence of nerve tortuosity. Axial T2-weighted images were used to evaluate for interruption without return, interruption with return, and deviation of the optic nerves; coronal T2-weighted images were used to assess lack of congruity. T2-weighted images in both planes were used to assess dilatation of the SAS. Hence, all parameters could not be assessed together at the same imaging section, but all could be present within the same nerve using the different imaging planes (Fig. 2). To systematically measure the SAS, the entire diameter of the nerve and sheath was measured 5–10 mm posterior to the globe in both axial and coronal planes; then, the optic nerve diameter at the same location was subtracted. An ROC curve analysis was used to determine the optimal cutoff value for the SAS dilatation parameter in both the axial and the coronal planes.

**Contrast Enhancement**

Optic nerves in patients with NF1 were assessed after contrast material administration. All nerves that displayed contrast material uptake were considered to be enhancing regardless of the pattern (i.e., subtle, focal, or diffuse) or segment along the nerve where it occurred.

**Scoring System**

A composite score of maximum diameter for the optic nerve in NF1 with and without ONG and tortuosity was designed, and the performance of the model was analyzed using an ROC curve. The sensitivity and specificity for detecting ONG at 2-point intervals in the scoring system were calculated.

**Statistical Analysis**

All measurements are expressed as means ± standard error. Optic nerve diameter and SAS dilatation were analyzed using a nonparametric Kruskal-Wallis test, and the post hoc analysis was corrected for multiple comparisons using the Dunn-Bonferroni method. Interrater agreement for tortuosity parameters was determined using the Cohen kappa coefficient.

---

**Fig. 2**—Typical MR images of orbit for patients with neurofibromatosis type 1 (NF1) with optic nerve glioma (ONG), patients with NF1 but not ONG, and control subjects. A and B, 31-month-old boy with NF1 and ONG. Axial T2-weighted image (A) shows thickening and hyperintense signal throughout right optic nerve and in left midsegment. Right optic nerve shows angular deviation, and left optic nerve shows interruption with return. Coronal T2-weighted image (B) shows lack of congruity of optic nerves and bilaterally dilated subarachnoid space (SAS). C and D, 56-month-old boy with NF1 but not ONG. Axial (C) and coronal (D) T2-weighted images show thickening of both optic nerves with deviation of left optic nerve (C) and mild dural ectasia of optic sheath (D). E and F, 6-year-old girl with nystagmus. Axial (E) and coronal (F) T2-weighted images show normal diameter and signal intensity of optic nerve on both sides without signs of tortuosity (E) and normal SAS bilaterally with proper congruity of optic nerves (F).
SAS dilation data were further analyzed using an ROC curve to determine an optimal cutoff value. Tortuosity data were categoric in nature and analyzed using a Pearson chi-square test. A nonparametric Spearman rho coefficient was calculated to assess correlation between variables. The variance inflation factor was used as a test for multicollinearity among tortuosity parameters. An ROC curve analysis was used again to test the performance of the scoring criteria in separating NF1 from NF1 without ONG. Linear and ordinal regression were used to test for effect of age on both the size metric and the scoring system. All statistical analyses were performed using SPSS software (version 23, IBM).

Results
A total of 144 children (111 with NF1, 33 without) who satisfied the inclusion criteria underwent MRI of the orbits at Montreal Children’s Hospital during the study period. Of the 111 patients with NF1, 60 were boys and 51 were girls. Of the 33 children without NF1, 19 were boys and 14 were girls. We assessed 222 nerves (71 with ONG and 151 without) in patients with NF1 and 66 nerves in healthy control subjects. Mean age ± SD when MRI of the orbits was performed was 3.6 ± 2.7 months (range, 4–212 months) in control subjects and was not significantly different among the three groups (K diagnose(2,288) = 5.842, p = 0.26). We found no significant associations between sex and study group; female patients accounted for 42% of nerves in patients with NF1 and ONG as well as nerves in control subjects and 48% of nerves in patients with NF1 but without ONG ($\chi^2 = 2.71, p = 0.26$).

The optic nerve diameter was assessed at eight locations in both the axial and coronal planes (Table 1). The diameter at each location was compared between control subjects, patients with NF1 without ONG, and patients with NF1 with ONG using the Kruskal-Wallis test. Diameter was significantly different at every location that was assessed (Table 1). Post hoc analysis revealed that diameters in patients with NF1 and ONG were significantly larger than those in either of the other groups for all the locations (all $p < 0.001$).

Further, the diameter was found to be significantly larger in patients with NF1 but not ONG compared with control subjects for measurements taken at the prechiasmatic level in both the axial and coronal planes ($p \leq 0.004$), midsegment and retroocular levels in the coronal plane ($p < 0.001$), and the intracanalicular level in the axial plane ($p < 0.001$). The mean maximal diameter ± SD for each control nerve in the coronal plane was found to be 3.3 ± 0.41 mm; thus, 3.7 mm and 4.1 mm correspond to the first and second SDs. In the axial plane, the mean maximal diameter of the optic nerve was 3.1 ± 0.39 mm, so 3.5 mm and 3.9 mm correspond to the first and second SDs above the mean. The mean of the maximal control diameter plus 1 and 2 SDs were used as cutoff values for the size criteria in the combined scoring system; they were compared with the maximal individual optic nerve diameter at each nerve.

Optic nerve tortuosity was assessed independently by two radiologists, and the interrater agreement and kappa coefficient were subsequently determined for each parameter. All criteria had high interrater agreement (intersection with no return, 93% agreement, $\kappa = 0.81$; intersection with return, 98% agreement, $\kappa = 0.92$; axial deviation, 98% agreement, $\kappa = 0.94$; dilated SAS, 94% agreement, $\kappa = 0.87$; increased curvature, 99% agreement, $\kappa = 0.96$; lack of congruity, 98% agreement, $\kappa = 0.93$). Furthermore, each of the tortuosity parameters was highly and significantly associated with ONG in patients with NF1 (Fig. 2 and Table 2). A bivariate correlation matrix of the score variables showed that no two variables had a high

| TABLE 2: Percentage of Different Optic Nerve Tortuosity Parameters in Patients With Neurofibromatosis Type 1 | Neurofibromatosis Type 1 | Without Optic Nerve Glia (% | Without Optic Nerve Glia (% | $\chi^2$ | $p$
|-----------------|-------------------------|---------------------------|---------------------------|-------|-------|
| Parameter       | With Optic Nerve Glia (%) | With Optic Nerve Glia (%) | With Optic Nerve Glia (%) | $\chi^2$ | $p$
| Interruption    | 31/71 (43.7) | 30/151 (19.9) | 13.7 | < 0.001 |
| Return          | 28/71 (39.4) | 33/151 (21.5) | 16.0 | < 0.001 |
| Axial deviation | 34/71 (47.9) | 35/151 (23.2) | 13.8 | < 0.001 |
| Dilated subarachnoid space | 51/71 (71.8) | 34/151 (22.5) | 49.7 | < 0.001 |
| Coronal         | 54/71 (76.1) | 54/151 (35.8) | 31.4 | < 0.001 |
| Subjective      | 40/71 (56.3) | 54/151 (35.8) | 8.38 | < 0.001 |
| Lack of congruity | 32/71 (45.1) | 31/151 (20.5) | 14.3 | < 0.001 |
| Increased sagittal curvature | 24/44 (54.5) | 28/116 (24.1) | 13.4 | < 0.001 |
| Combined five parameters | 5/71 (7.0) | 1/151 (0.7) | 66.3 | < 0.001 |

**TABLE 1: Mean Optic Nerve Diameter in Patients With Neurofibromatosis Type 1 With and Without Optic Nerve Glioma and in Healthy Control Subjects**

| Parameter       | Neurofibromatosis Type 1 | Without Optic Nerve Glia (%) | With Optic Nerve Glia (%) | $K_{\text{diagnose}(2,288)}$ | $p$
|-----------------|-------------------------|---------------------------|---------------------------|-----------------------------|-------|
| Mean Diameter (mm) | With Optic Nerve Glia (n = 71) | With Optic Nerve Glia (n = 151) | Control Subjects (n = 86) | $\chi^2$ | $p$
| Axial            | 3.1 ± 0.08 | 2.5 ± 0.04 | 2.4 ± 0.05 | 59.4 | < 0.001 |
| Midsegment       | 3.0 ± 0.13 | 2.1 ± 0.03 | 2.0 ± 0.05 | 71.0 | < 0.001 |
| Intracanalicular | 2.5 ± 0.11 | 1.7 ± 0.04 | 1.4 ± 0.03 | 103.2 | < 0.001 |
| Prechiasmatic    | 5.3 ± 0.21 | 3.7 ± 0.05 | 3.1 ± 0.05 | 127.5 | < 0.001 |
| Coronal          | 3.4 ± 0.08 | 2.8 ± 0.05 | 2.6 ± 0.05 | 59.4 | < 0.001 |
| Midsegment       | 3.4 ± 0.14 | 2.3 ± 0.04 | 2.0 ± 0.05 | 88.7 | < 0.001 |
| Prechiasmatic    | 4.3 ± 0.19 | 3.1 ± 0.04 | 2.9 ± 0.04 | 86.9 | < 0.001 |
| Chiasmatic       | 4.8 ± 0.21 | 3.4 ± 0.05 | 3.1 ± 0.06 | 61.5 | < 0.001 |
correlation (Spearman rho coefficient range, 0.08–0.64), so combinations of tortuosity parameters had the highest chi-square coefficients. The five-parameter combination excluded the increased curvature parameter, which had values missing because the 3D sequence was not part of the standard MRI protocol in some of the examinations evaluating the optic nerves. The parameter of increased curvature in the sagittal plane could not be evaluated in 71 nerves, corresponding to 38% of all those in patients with NF1 and ONG, 23% of nerves in patients with NF1 without ONG, and 15% of all control subjects. Given that the tortuosity parameters were not correlated or collinear (all variance inflation factors < 1.8), arbitrarily removing data points to include all six parameters would likely affect the sensitivity and specificity of the other five. Thus, to avoid introducing bias, we decided to not include the curvature parameter in the final composite score and to instead include all the subjects.

Because of limited agreement among radiologists regarding the presence or absence of SAS dilatation in a previous study [9], it was quantified in this dataset using an axial and coronal measurement at a single location. The SAS was found to be significantly larger in patients with NF1 and ONG (axial, 2.3 ± 0.09 mm; coronal, 2.2 ± 0.08 mm) than in those with NF1 without ONG (axial, 1.7 ± 0.03 mm; coronal, 1.6 ± 0.03 mm) and control subjects (axial, 1.5 ± 0.08 mm; coronal, 1.5 ± 0.08 mm) (K_{axial(2,288)} = 58.3, p < 0.001; K_{coronal(2,288)} = 44.2, p < 0.001). ROC curves of SAS dilatation measurements had an AUC of 0.79 ± 0.03 axially and 0.76 ± 0.03 coronally. The curves were used to determine a cutoff value for the SAS dilatation; values of 2.0 mm in the axial plane (sensitivity, 71.8%; specificity, 77.5%) and 1.8 mm in the coronal plane (sensitivity, 76.1%; specificity, 64.2%) were chosen as cutoff values. The SAS dilatation cutoff as measured in the axial plane was used in the combined scoring criteria because it was the most highly associated with the group of patients with NF1 and ONG (Table 2).

Contrast enhancement was seen in 26 of 70 clinically diagnosed ONGs; none of the

---

**TABLE 3: Sensitivity and Specificity of the Combined Scoring Criteria**

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Axis</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>Axial</td>
<td>90</td>
<td>87</td>
<td>83</td>
<td>62</td>
<td>35</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>Axial</td>
<td>54</td>
<td>60</td>
<td>80</td>
<td>90</td>
<td>97</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>Coronal</td>
<td>85</td>
<td>79</td>
<td>70</td>
<td>54</td>
<td>28</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>Coronal</td>
<td>74</td>
<td>80</td>
<td>89</td>
<td>95</td>
<td>99</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

---

**Fig. 3**—Summary of scoring system based on tortuosity parameters and maximum nerve diameter. ONG = optic nerve glioma.
155 nerves in patients with NF1 without ONG showed enhancement. Given the high specificity for contrast enhancement in this group (100%), an optic nerve that shows contrast enhancement may be considered an ONG and does not need to be analyzed using the more detailed scoring criteria (Fig. 3). However, the low sensitivity of contrast enhancement for ONG (37%) highlights the rationale behind establishing scoring criteria that include other radiologic features.

To create a simple scoring system, only the maximal optic nerve diameter regardless of location was used despite significant enlargement along the whole length of the nerve in patients with ONG (Table 1). We believed that measuring only at the maximum diameter along the optic nerve rather than measuring at several discrete points and then calculating means would be more practical. Furthermore, the rationale for using 1 and 2 SDs of the maximum diameter of control subjects rather than a binary variable approach was to increase the sensitivity of the size parameter in the final scoring system.

Each tortuosity parameter was given a score of 1 if it was present, for a maximum score of 5. Nerve diameters in patients with NF1 were compared with the first and second SD above the mean maximum values in control subjects. Values that were at or above the first SD for control nerves were given a value of 2.5 and those at or above 2 SDs received a score of 5. These values were chosen so that nerve diameter criteria would have the same weight as the tortuosity criteria in the combined scoring system. The combined criteria had a maximum value of 10. ROC curves were calculated for each scoring system (Fig. 4); the AUC was 0.91 ± 0.03 for coronal and 0.89 ± 0.03 for axial planes, respectively. The sensitivities and specificities at discrete points, patient age could have affected either the optic nerve diameter or the overall scoring system. To determine if this was the case, a linear regression analysis was done and showed that age has a very low coefficient of determination in relation to size at all locations measured ($r^2$ range, 0.000–0.013). Furthermore, we assessed whether the combined score was affected by the age of the patients. Given that the score data were ordinal in nature, an ordinal regression was used with score as the dependent variable, diagnosis as the independent variable, and age as a covariate. The results from axial score model indicate that age does not affect the score.

The age covariate has a Wald statistic equal to 0.388 ($p = 0.534$). Similarly, the coronal scoring system, also analyzed with ordinal regression, was not significantly affected by age with a Wald statistic equal to 1.211 ($p = 0.271$). Thus, we conclude that the score metrics or size cut-offs do not need to be adjusted for age.

**Discussion**

Patients with NF1 are at high risk of developing ONGs, which can lead to optic nerve compression, atrophy, and vision loss if not appropriately diagnosed and treated [15, 16, 28]. No objective scoring criteria are available to accurately diagnose ONG in these patients, and there are many institutional variations. Nerve enlargement and tortuosity, previously described radiologic findings on MRI of the orbit in patients with NF1 and ONGs, were reviewed in cases at our institution from 2003 to 2016 [25, 27].

Studies have shown that an optic nerve diameter of 3.9 mm corresponds to 2 SDs above the mean maximum diameter in healthy control subjects; that value was reproduced in our dataset [25, 29]. Further, although only the maximum value of each nerve was used in the final scoring system for simplicity, the optic nerve was significantly enlarged in patients with NF1 and ONG at all measured locations compared with the other two groups (Table 1). However, using only optic nerve diameter as a diagnostic criterion may lead to misdiagnosis because patients with NF1 may have enlargement of the optic nerve without glioma (Table 1), and early gliomas may have minimally increased diameter.

To provide a more comprehensive evaluation of the optic nerves, the association between ONG and the presence of optic nerve tortuosity was also studied. Little is known about the pathogenesis of optic nerve tortuosity in NF1, but it may be a precursor to the formation of gliomas and is associated in ONG in patients with NF1 [27, 30–33]. Previously proposed optic nerve tortuosity parameters were validated in this study [27] (Table 2). Although these parameters are reproducible, few attempts have been made to quantify them, and none have done so without requiring specialized software [33]. The measurement of dural ectasia or SAS dilatation in our study emerged as a prominent feature of ONG in patients with NF1 in our study. Using an ROC curve–derived cutoff for this parameter (2.0 mm and 1.8 mm in the axial and coronal planes, respectively) differ-
ented ONG from absence of ONG better than a radiologist’s appraisal of SAS dilatation without measurement (Table 2).

Both optic nerve diameter data and tortuosity parameters were combined into a simple scoring system that was found to be highly reliable in detecting the presence of optic nerve glioma in patients with NF1 (Fig. 2, Table 3). Although scoring systems such as ours may someday be replaced by machine learning algorithms, at this time such algorithms have several limitations. They require very large datasets, which are not available for patients with NF1; they rely on specialized software; and until they are widely accepted, they will need to be verified by a radiologist [34]. In comparison, the proposed scoring system based on 288 MRI studies of the orbits that have undergone blinded review by two different radiologists is easy to learn and use, requires no special software, and can be tested on available datasets.

In conclusion, this scoring system is an important first step in improving the diagnostic yield of MRI of the orbits in patients with NF1, but future prospective, multicenter studies or the retrospective application of these criteria on datasets acquired at other institutions are needed for validation and determination of clinically relevant cutoff scores. Broadly, our data suggest that scores of 4 or less are not suggestive of ONG, scores higher than 4 and less than 8 are suggestive of glioma, and scores of 8 or more are likely to be ONG in patients with NF1 (Fig. 3, Table 3). If this scoring system is proven to be effective in future studies, it may obviate contrast-enhanced studies, thereby reducing the number of MRI sequences and avoiding potential risks of gadolinium deposition, and could augment current clinical screening programs [35–37].

References