Computed Tomography Characteristics of Non-Syndromic Craniofacial Fibrous Dysplasia

Yu-Ray Chen, MD; Fen-Hwa Wong[1], PhD; Chun Hsueh[2], MD; Lun-Jou Lo, MD

Background: Fibrous dysplasia is a benign fibro-osseous tumor of bones commonly involving the craniofacial region. Computed tomography (CT) imaging study of the disease is useful for evaluation and treatment planning. However, few studies have evaluated such large patient series.

Methods: A total of 46 patients with complete medical records and CT images was included in this study. All of these patients were non-syndromic, had fibrous dysplasia involving only the craniofacial region, and had no skin pigmentation or other evidence of endocrine problems. Data analyses were performed on the clinical manifestations, time of onset, signs and symptoms, involvement of cranial and facial bones, and CT appearance of the tumors in this patient group.

Results: Painless swelling was the chief clinical problem in 78% of patients, followes by dental malocclusion in 22%. Onset of the disease was reported to have occurred before 6 years of age in 34%, between 6 and 10 years in 27%, and older than 10 years in 39% of patients. Extreme timings such as onset at infancy or older than 20 years of age were also noted. The average number of bones involved was 3.2 bones per patient. Involvement of more than one craniofacial bone occurred in 70% of patients. The maxilla, orbital, and frontal bones were most commonly involved. CT images appeared sclerotic or homogenous in 34%, mixed white and dark or heterogenous in 55%, and cystic in 11%. A correlation between the age of onset of the disease and the number of bones involved was not observed.

Conclusions: Findings of this study demonstrate that craniofacial fibrous dysplasia displays a wide spectrum of clinical behaviors. CT imaging generally revealed extensive involvement of the tumor in the craniofacial region.
(Chang Gung Med J 2002;25:1-8)

Key words: craniofacial fibrous dysplasia, computed tomography imaging.

Fibrous dysplasia of the bone is a fairly common, well-recognized, locally circumscribed, slowly progressive, benign disorder of fibro-osseous tissues. Although virtually all bones can be affected, the cra-nial and facial bones are most frequently involved. During the disease process, normal bone is replaced by an abnormal proliferation of fibrous tissue comprised of spindle cells and poorly formed bony tra-

beculae of woven bone. Fibrous dysplasia can appear as an isolated disease or in association with endocrine disorders and skin pigmentation, i.e., the McCune-Albright syndrome. Factors predisposing the development of fibrous dysplasia remain unknown. Among the reported causative factors are abnormal development of undifferentiated osteoplastic mesenchymal tissue,[1] disordered metabolism of calcium and phosphorus,[2] hyperplasia of osteoblasts,[3] and abnormal reparative processes following bone injury.[4,5] Recently, activating mutations of Gs protein were found in lesions of fibrous dysplasia.[6-8] G proteins are cellular signal transducers, and Gs is a stimulatory G protein. Mutations present in a mosaic pattern, with the greatest number in the most abnormal areas of affected tissues. It is not a germline but rather a post-zygotic somatic mutation. These genetic findings are important for clinical investigations of the biological behavior of fibrous dysplasia. However, there is a paucity of these types of studies for this disease.

Fibrous dysplasia is usually not manifested at birth. It becomes noticeable years later as a benign swelling in the tumor region. It has been reported that 70% of cases are monostotic, that is, involving only one bone or contiguous bones, while 30% of cases are polyostotic.[4] Almost all patients with extensive polyostotic forms of the disease have skull involvement,[9-12] while most patients with craniofacial bone involvement have the monostotic form of the disease.[13,14] As we have extensive experience in treating craniofacial fibrous dysplasia,[15-21] we present a series of non-syndromic cases and study its clinical behavior.

METHODS

During the past 20 years, more than 100 patients with craniofacial fibrous dysplasia were treated at the Craniofacial Center, Chang Gung Memorial Hospital, Taoyuan. Forty-six patients were selected from this group because they had adequate medical records and computed tomography (CT) imaging data. Patients were excluded from the study if they were syndromic, had documented extra-craniofacial involvement, or had skin pigmentation or other evidence of endocrine disease. Clinical information analyzed included signs and symptoms related to the disease, and the time of its onset or observations of

patients or their parents.

CT images in the bone window were carefully reviewed to determine the appearance and the extent of involvement of the tumor. The CT appearance of fibrous dysplasia was categorized as sclerotic if it was homogenously white, heterogeneous if it showed mixed with the white and dark contents in CT images of the lesion, or cystic if one or more cysts were present within the lesion. The involved cranial and facial bones were differentiated and recorded. They included the frontal, occipital, parietal, temporal, orbital, zygoma, maxilla, mandible, central skull base, nasoethmoid, and sphenoid. It should be noted that the central skull base contains areas surrounding the sellae, clivus, and the great foramen, which are parts of the sphenoid, temporal, and occipital bones, respectively. In CT images, accurate separation of individual anatomical bones in the central skull base is diffucult.

RESULTS

Among the 46 patients, 20 were male and 26 were female. Positive family history of the disease was denied by all of these patients. The chief complaint was painless swelling in 78% and malocclusion in 22% of patients. Two patients complained of pain in the lesion: 1 had a huge facial tumor with ulceration, and the other suffered periodic pain in the orbital region synchronous with her menstrual cycle. In the latter patient, a cystic change in the lesion was found on CT examination. Eight patients complained of visual problems, and exhibited decreased visual acuity and/or diplopia. None of the patients complained of numbness in the craniofacial region, and none developed a malignancy during the follow-up period.

Regarding the first onset or first observance of craniofacial fibrous dysplasia, the reported timing ranged from birth to 27 years of age. Of these, 34% were noted at or before 6 years of age, 27% between 6 and 10 years of age, and 39% at older than 10 years of age. In only one patient was the tumor reportedly observed during infancy. The tumor was first noticed after 20 years of age in 7% of patients. Some patients in this study reported a secondary tumor which appeared several years after the first onset, with or without prior surgical treatment of the first lesion.

Multiple views of CT images in the bone window were used to evaluate the location and extent of the tumor in the craniofacial region. In general, tumors involved unilateral rather than bilateral regions, or the midline area, creating cranial and facial asymmetry. The left side was twice as often involved as the right side. The lesion usually involved more than one bone, and its progression was not limited by craniofacial sutures (Tables 1, 2). The average number of bones involved was 3.2 bones per patient. CT images showed continuous tumor expansion across the sutures without signs of interruption. The maxilla, orbital, and frontal bones were the most-common structures involved. However, the central skull base and sphenoid bones also exhibited a significant incidence of tumor involvement. These sites were difficult to diagnose using conventional X-ray. Single-bone involvement comprised only 30% of cases in this study. Among these 10 involved the maxilla, 2 the mandible, one the frontal bone, and one the nasoethmoid bone. On the CT images, the tumor appeared homogenous or sclerotic in 34% (Fig. 1), heterogeneous or with a mixed white-and-dark appearance in 55% (Fig. 2), and cystic in the remaining 11% of the sample (Fig. 3). Cysts were small or large, and in some cases the cystic degeneration had occurred rapidly according to the clinical presentation and serial CT imaging

Table 1. Distribution of Osseous Involvement of Craniofacial Fibrous Dysplasia in 46 Patients

	No. of time involved	Percentage (%)
Frontal	21	13.8
Occipital	0	0
Parietal	2	1.3
Temporal	13	8.6
Orbital	24	15.8
Zygoma	13	8.6
Maxilla	27	17.8
Mandible	7	4.6
Central skull base	16	10.5
Nasoethmoid	15	9.9
Sphenoid	14	9.2
Total	152	100

Table 2. Types of Osseous Involvement of Craniofacial Fibrous Dysplasia in 46 Patients

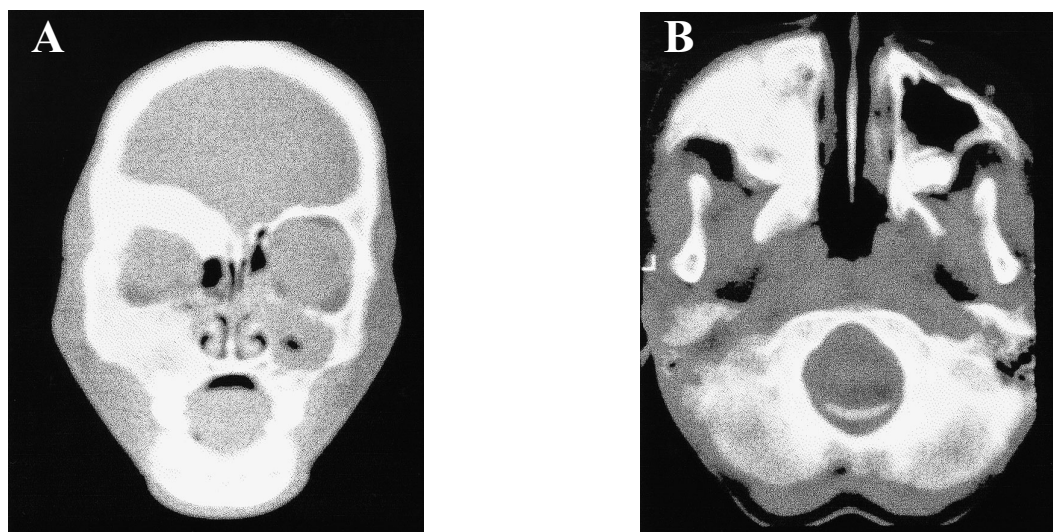| Involvement	Number of patients	Percentage (%)
Single bone	14	30
2 to 3 bones	15	33
4 to 6 bones	12	26
7 to 9 bones	5	11
Total	46	100

Fig. 1 CT images of coronal (A) and axial (B) views in the bone window showing fibrous dysplasia involving the right maxilla, zygoma, orbital, and sphenoid bones. The tumor appeared sclerotic and white.
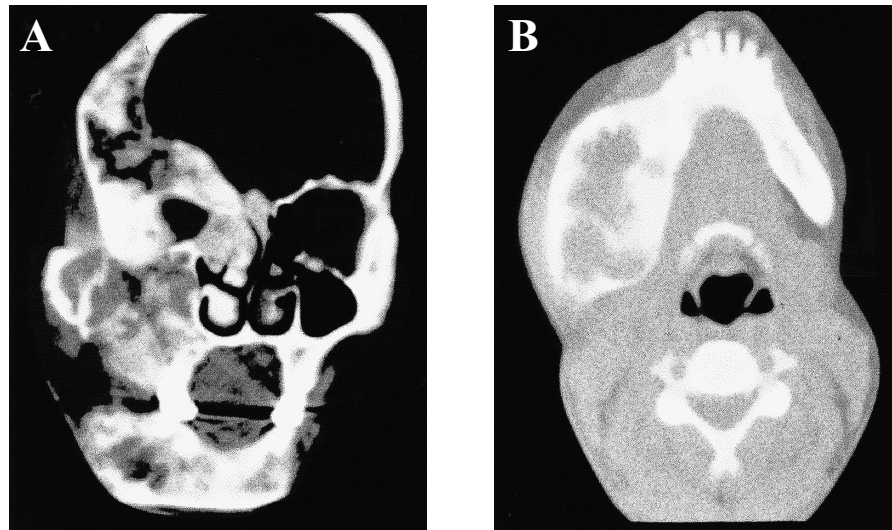
Fig. 2 CT images of coronal (A) and axial (B) views in the bone window showing fibrous dysplasia involving the right maxilla, zygoma, orbital, temporal, nasoethmoid, and mandibular bones. The tumor is heterogeneous in nature with mixed white-and-dark structures.
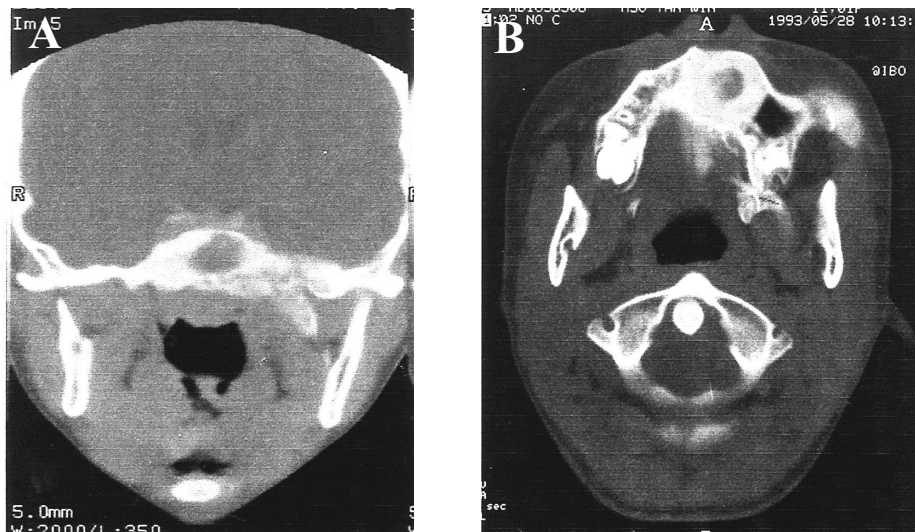

Fig. 3 CT images of coronal (A) and axial (B) views in the bone window showing fibrous dysplasia involving the skull base and maxilla. Cystic change can be seen in both regions.

examinations. The average number of bones involved was 4.07 in patients with disease onset before 6 years of age, 3.0 in patients with onset between 6 and 10 years, and 3.19 in patients with onset after 10 years. There was no correlation between the age of the patient at onset of the disease and the number of bones involved.

DISCUSSION

The incidence of craniofacial fibrous dysplasia is not known. There are sporadic case reports and occasional large patient series seen in the literature.[22,23] We believe that a significant portion of patients with the disease remain undiagnosed. This group of patients with subclinical fibrous dysplasia have smaller tumors in deeper locations that do not manifest clinical signs or symptoms. The tumor may remain undetected throughout the lifetime of the patient. We had the experience of treating an adult patient with facial fractures, whose CT scans revealed an incidental "silent" fibrous dysplasia in the right zygoma area. The usual natural history of craniofacial fibrous dysplasia is a finding of painless swelling many years after birth. Growth of the tumor occurs during a certain period, usually before maturation of the craniofacial skeleton, and then the tumor becomes clinically quiescent. Its typical clinical presentations are local swelling and asymmetry in the craniofacial region. In our study, 1/3 of patients reported the occurrence of the disease in childhood. However, 39% of patients observed its onset at older than 10 years of age, and a small portion experienced a late onset of the disease at older than 20 years of age. It is interesting to note that there was no correlation between the onset of disease and the extent of bony involvement.

Functional disturbances are not common in craniofacial fibrous dysplasia. When manifested, they are mainly related to visual disturbances and dental malocclusion resulting from tumor involvement of the periorbital regions, and maxilla or mandible, respectively. Sudden or gradual loss of visual acuity is a serious complication of the disease, and should be managed with aggressive surgical intervention.[18,24,25] Regular follow-up with ophthalmologic and CT imaging examinations are mandatory for early diagnosis, management, and prevention of visual problems. The treatment principles of craniofacial fibrous dysplasia have been categorized as aggressive excision, conservative shaving, or observation, depending on the involvement of the different craniofacial zones.[17] Surgical intervention is indicated as early as symptoms and signs occur. The principles of surgical treatment are based on the zones of involvement: total excision of a tumor of fronto-orbital, zygoma, and upper maxillary origin and primary bone reconstruction; conservative excision on hair-bearing skull, central cranial base, and tooth-bearing bones; and optic canal decompression in patients with orbital dysplasia and decreasing visual acuity.

There are few reports of CT imaging studies of craniofacial fibrous dysplasia. It is our experience that imaging examinations are important for monitoring of the tumor progression, formulating a treatment plan, and for postoperative or longitudinal follow-up. Conventional X-rays only reveal the tumor as a patch of haziness.[26] Determination of the location and extent of the tumor on those films is difficult because of overlapping anatomical structures. CT scanning appears to be the best method for imaging fibrous dysplasia, although other imaging modalities such as magnetic resonance imaging, SPECT imaging, and gallium-67 uptake have been reported.[27-32] The average number of bones involved (3.2) indicates that the disease had already spread extensively by the time it was diagnosed. In this study, single bone involvement was found in only 30% of patients, with the highest incidence in the maxilla. Up to 70% of patients had 2 or more craniofacial bones affected, most commonly the maxilla, orbital, and frontal bones (Tables 1, 2). Possible reasons for the apparently high frequency of involvement of these bones may be their more noticeable location and the earlier appearance of facial deformity. In contrast, it also should be noted that the deeper and more clinically inaccessible areas, such as the central skull base, nasoethmoid, and sphenoid bone, were not infrequently affected by the disease process (Table 1).

The wide spectrum of clinical behaviors of craniofacial fibrous dysplasia is reflected not only in the location and extent of the tumors but also in the CT findings. CT imaging showed the lesions to be of homogenous or heterogeneous density, or cystic in nature. More than 1/2 of the patients had tumors with heterogeneous density, indicating a mixture of calcified/ossified and fibrous tissues within the tumor mass. This finding was confirmed by microscopic examination of tumor specimens. Cystic degeneration of a tumor is a phenomenon not yet well understood, and it was very uncommon.[33,34] Cystic changes in the lesions of our patients were incidental findings that were accompanied by com-

plaints, such as sudden visual loss and periodic orbital pain.

The findings in this study provide fundamental information for understanding the tumor biology of fibrous dysplasia. Recently, cellular signal transduction errors were found to be present in fibrous dysplasia. Activating mutation of the Gs protein was detected to exist in the tumor but not normal bone.[6-8] Our preliminary study supports these findings. Further study on erroneous cellular signal transduction may help explain the pathogenesis and clinical behavior of this disease.

Acknowledgements

REFERENCES

1. Lichtenstein L, Jaffe HL. Fibrous dysplasia of bone. Arch Pathol 1942;33:777-816.
2. Murray RC, Kirkpatrick HJR, Forrai E. Case of Albright's syndrome (osteitis fibrosa disseminata). Br J Surg 1946;34:48-57.
3. Changus GW. Osteoblastic hyperplasia of bone. A histochemical appraisal of fibrous dysplasia of bone. Cancer 1957;10:1157-61.
4. Schlumberger HG. Fibrous dysplasia of single bones (monostotic fibrous dysplasia). Milit Surgeon 1947;99:504-27.
5. Simovic S, Klapan I, Bumber Z, Bura M. Fibrous dysplasia in paranasal cavities. J Otorhinolaryngol Relat Spec 1996;58:55-8.
6. Alman BA, Greel DA, Wolfe HJ. Activating mutations of Gs protein in monostotic fibrous lesions of bone. J Orthop Res 1996;14:311-5.
7. Ringel MD, Schwindinger WF, Levine MA. Clinical implications of genetic defects in G proteins: the molecular basis of McCune-Albright syndrome and albright hereditary osteodystrophy. Medicine 1996;75:171-83.
8. Marie PJ, de Pollak C, Chanson P, Lomri A. Increased proliferation of osteoblastic cells expressing the activating Gs alpha mutation in monostotic and polyostotic fibrous dysplasia. Am J Pathol 1997;150:1059-69.
9. Windolze F. Cranial manisfestations of fibrous dysplasia of bone. AJR Am J Roentgen 1957;58:51-63.
10. Harris WH, Dudley HR Jr, Barry JR. The natural history of fibrous dysplasia. J Bone Joint Surg (Am) 1962;44A:207-33.
11. Leeds N, Seaman WB. Fibrous dysplasia of the skull and its differential diagnosis. Radiology 1962;78:570-82.
12. Sassin JF, Rosenberg RN. Neurological complications of fibrous dysplasia of the skull. Arch Neurol (Paris) 1968;18:363-9.
13. Calderon M, Brady HR. Fibrous dysplasia of bone with optic foramina involvement. Am J Ophthalmol 1969;68:513-5.
14. Moore RT. Fibrous dysplasia of the orbit. Surv Ophthalmol 1969; 13: 321-34.
15. Munro IR, Chen YR. Radical treatment for fronto-orbital fibrous dysplasia: the chain-link fence. Plast Reconstr Surg 1981;67:719-30.
16. Chen YR, Fairholm D. Fronto-orbito-sphenoidal fibrous dysplasia. Ann Plast Surg 1985;15:190-203.
17. Chen YR, Noordhoff MS. Treatment of craniomaxillofacial fibrous dysplasia: how early and how extensive? Plast Reconstr Surg 1991;87:799-800.
18. Chen YR, Breidahl A, Chang CN. Optic nerve decompression in fibrous dysplasia: indications, efficacy, and safety. Plast Reconstr Surg 1997;99:22-30.
19. Cheng MH, Chen YR. Malignant fibrous histiocytoma degeneration in a patient with facial fibrous dysplasia. Ann Plast Surg 1997;39:638-42.
20. Szwajkun P, Chen YR, Yeow VK, Breidahl AF. The "Taiwanese giant": hormonal and genetic influences in fibrous dysplasia. Ann Plast Surg 1998;41:75-80.
21. Yeow VK, Chen YR. Orthognathic surgery in craniomaxillofacial fibrous dysplasia. J Craniofac Surg 1999;10:155-9.
22. Ruggieri P, Sim FH, Bond JR, Unni KK. Malignancies in fibrous dysplasia. Cancer 1994; 73:1411-24.
23. Xu D, Luan H, Zhan A, Feng W, Sun X, Meng F. Spontaneous malignant transformation of fibrous dysplasia. Chin Med J (Engl) 1996;109:941-5.
24. Saito K, Suzuki Y, Nehashi K, Sugita K. Unilateral extradural approach for bilateral optic canal release in a patient with fibrous dysplasia. Surg Neurol 1990;34:124-8.
25. Papay FA, Morales L Jr, Flaharty P, Smith SJ, Anderson R, WAlker JM, Hood RS, Hardy S. Optic nerve decompression in cranial base fibrous dysplasia. J Craniofac Surg 1995;6:5-10.
26. Obisesan AA, Lagundoye SB, Daramola JO, Ajagbe HA, Oluwasanmi JO. The radiologic features of fibrous dysplasia of the craniofacial bones. Oral Surg Oral Med Oral Pathol 1977;44:949-59.
27. Hoshi H, Futami S, Ohnishi T, Nagamachi S, Jinnouchi S, Murai N, Watanabe K. Gallium-67 uptake in fibrous dysplasia of the bone. Ann Nuclear Med 1990;4:35-8.
28. Casselman JW, De Jonge I, Neyt L, De Clercq C, D'Hont G. MRI in craniofacial fibrous dysplasia. Neuroradiol 1993;35:234-7.
29. Yano M, Tajima S, Tanaka Y, Imai K, Umebayashi M. Magnetic resonance imaging findings of craniofacial

fibrous dysplasia. Ann Plast Surg 1993;30:371-4.

30. Yao L, Eckardt JJ, Seeger LL. Fibrous dysplasia associated with cortical bony destruction: CT and MR findings. J Comput Assist Tomogr 1994;18:91-4.

31. Jee WH, Choi KH, Choe BY, Park JM, Shinn KS. Fibrous dysplasia: MR imaging characteristics with radiopathologic correlation. AJR Am J Roentgenol 1996;167:1523-7.

32. Jimenez CE, Moreno AJ, Pacheco EJ, Carpenter AL.

SPECT imaging in a patient with monostotic rib fibrous dysplasia. Clin Nucl Med 1996;21:491-3.

33. Taborelli A, Ballarini V, Monolo L, Dorizzi A. Cystic fibrous dysplasia of the skull presenting as an extradural mass. Case report. J Neurosurg Sci 1983;27:253-6.

34. Lucarelli MJ, Bilyk JR, Shore JW, Rubin PA, Yaremchuk MJ. Aneurysmal bone cyst of the orbit associated with fibrous dysplasia. Plast Reconstr Surg 1995;96:440-5.

≪Dflg≫ ,s˘'^C ' f¯ "ß'°†§–'..W¥""",,q,£´_.h.v„‡flS.x

‡fkR•　　fḷ"　　¹　`§　fl ′² ^„'œw

>I "G　　' f¯ "ß'°†§–'..W¥"<O/@"　' f""¤}'°,~&F¡A˘'^C<O–'¤£fn o""‡ƒ ¡A„q,£´_.h˜Æ
...v ¸<d„ ƒ„flf"" ßƒ »P"v ł>p e≪ ƒ‡　§U¡A Mƒ / ˜m/W'|fl°¥F, † "" ßƒ ‡ł§i¡A'
¥‡ƒfb‡o¶ ¸ᵃ¤ᶜ§ > ƒ<¶ ¸Œfi˜/ "R¤ `{§ " †{'M„q,£´_.h.v„‡flS.x¡C

/Ł "KG　　§ > ¬q,Œfi˜fw ƒ<¶ ƒ@　　46 > flf¤　/ "R¡Aflf¤ ƒ<¶ ""...—• '<O‡ o'°ƒb˘'^C‡ƒ ""¡A≪D
flg≫ ,s""¡A¤§ƒ‡¥ &§ƒ fl †§–'/¸/"/ "cflefIf""¡A¤^¥Bƒ‡» ¥ ""flf œ O¿ 'M„q,£´_.h
¸<d"",¡C,Œfi˜""/ "R¥]<A`{§ ,Œ T¡A oflf ƒ~˜ ¡A`{§ flg"<¡A˘'^C‡ƒ ¤ ≪I¥˙"" '
f¡A¥¥/¸,q,£´_.h.v„‡""flS.x¡C

† "G　　¥D>n`{§ ˆDƒb L h'°< _""ßß　　78%¡A⁄œ ƒ≪ƒX‡§–'" ßß　　22%¡C‡˜/@ƒ, cflf""‡ł§iƒb
6•‡‡k̄e""ßß　34%¡A¶' 6ƒ 10•†""ßß 27%⁄̆ƒ 10•‡‡k̄Æ cflf""≪hƒß　39%¡Aßfi cflf ƒ~
˜ ƒp ƒ¤ ¸•`'M　20•‡‡k̄Æ""/]ƒ‡ o‡{¡CœCƒ flf/‡¥>§¡ƒ‡　　3.24¶ ˘'^C ' f¤ ƒ„flf≪Ifi'¡A
70%""flf/H¤ ≪I¥˙ ' f<O/@¶ ¥‡/W¡A‡ –'¤£""¤ ¥ '<O/WˆE¡A‡•† ¡A'M≪eˆB¡C,q,£´_
..h.v,‡§e‡ł ¥ ƒ " ßß　　34%¡A§e‡{¶‡^œ"<‡VƒXƒ " ßß　　55%⁄̆ƒ 11%¤£n'°¯ /¯¡C cflf
ƒ~ »P ' f≪I¥˙...˘¥ /§¶¡¤§ƒ‡< ^ ‡s¡C

†‰G　　f„¸ᵃ¤ᶜs †"G¯ᵃ¥ ˘'^C ' f¯ "ß'°†§–'..W¥"§e‡{..e.s""`{§ ƒ < " †{¡A„q,£´_.h.v„‡
≪h< ¥Xƒ„flf ƒb˘'^C‡ƒ ""≪I¥˙ <J†'¥B.s¡C
("‡' ´≫x　2002;25:1-8)

^`fr¡G　˘'^C ' f¯ "ß'°†§–'..W¥"¡A„q,£´_.h.v„‡¡C