

## 研究成果の刊行に関する一覧表

1. Ito Z, Harada A, Matsui Y, Takemura M, Wakao N, Suzuki T, Nihashi T, Kawatsu S, Shimokata H, Ishiguro N. Can you diagnose for vertebral fracture correctly in plain X-ray? *Osteoporos Int* 17: 1584-91, 2006.
2. Harada A, Matsui Y, Okuizumi H, Wakao N, Suzuki T, Ito Z. Percutaneous vertebroplasty for elderly patients with unhealed osteoporotic spinal fractures. *Geriatr Gerontol Int* 6: 174-181, 2006.
3. Sakamoto K, Nakamura T, Hagino H, Endo N, Mori S, Muto Y, Harada A, Nakano T, Yamamoto S, et.al. Report on the Japanese Orthopaedic Association's 3-year project observing hip fractures at fixed-point hospitals. *J Orthop Sci* 11: 127-134, 2006.
4. Sakamoto K, Nakamura T, Hagino H, Endo N, Mori S, Muto Y, Harada A, Nakano T, et al. Effects of unipedial standing balance exercise on the prevention of falls and hip fracture among clinically defined high-risk elderly individuals: a randomized controlled trial. *J Orthop Sci* 11: 467-472, 2006.
5. Asaba Y, Hiramatsu K, Matsui Y, Harada A, Nimura Y, Katagiri N, et al. Urinary  $\gamma$ -glutamyltransferase (GGT) as a potential marker of bone resorption. *Bone* 39: 1276-1282.
6. Ito Z, osawa Y, Matsuyama Y, Aoki T, Harada A, Ishiguro N. The recurrence of hypertrophic spinal pachymeningitis. *J Neurosurg Spine* 4: 509-513, 2006.
7. Hanai Y, Tokuda H, Takai S, Harada A, Ohta T, Kozawa O. Minodronate suppresses prostaglandin  $F_{2\alpha}$ -induced Vascular Endothelial Growth Factor Synthesis in Osteoblasts. *Horm Matab Res* 38: 152-158, 2006.
8. 原田敦. 骨粗鬆症・骨折の合併症とQOL 1. 大腿骨頸部骨折 骨粗鬆症診療ハンドブック改訂4版 医薬ジャーナル社 156-165, 2006.
9. 原田敦、山本精三、倉都滋之、岩瀬敏樹、井上喜久男、佐々木康夫、田中孝昭、他 老年医療におけるControversy 2. 超高齢者骨粗鬆症はビスフォスフォネートで治療すべきである (Con) 日本老年医学会雑誌 43: 459-461, 2006.
10. 原田敦. 運動器不安定症と今後の展開 整形・災害外科 50: 27-35, 2006.
11. 原田敦. 高齢者の大腿骨頸部骨折と転倒予防ー骨粗鬆症、ヒッププロテクターを含むー整形外科 57: 1635-1642, 2006.
12. 原田敦. 運動指導・転倒防止のリハビリテーション 日本臨床 特集：高齢者骨

疾患 64: 1687-1691, 2006.

13. 原田敦. 骨粗鬆症、骨折における性差医療 性差と医療 3: 409-412, 2006.
14. Takai S, Tokuda H, Matsushima-Nishiwaki R, Hanai Y, kato K, Kozawa O. Phosphatidylinositol 3-kinase/Akt Plays a role in sphingosine 1-phosphate-stimulated HSP27 induction in osteoblasts. J Cell Biochem 98: 1249-1256, 2006.
15. Hanai Y, Tokuda H, Ishisaki A, Matsushima-Nishiwaki R, Nakamura N, Yoshida M, Takai S, Kozawa O. Involvement of p44/p42 Map kinase in insulin-like growth factor-I-induced alkaline phosphatase activity in osteoblast-like MC3T3-E1 cells. Mol Cell Endocrinol 251: 42-48, 2006.
16. Hanai Y, Tokuda H, Ohta T, Matsushima-Nishiwaki R, Harada A, Kato K, Kozawa O. Phosphatidylinositol 3-kinase / Akt Auto-regulates PDGF-BB-Stimulated interleukin-6 synthesis in osteoblasts. J Cell Biochem 99: 1564-1571, 2006.
17. Takai S, Tokuda H, Yoshida M, Yasuda E, Matsushima-Nishiwaki R, Harada A, Kato K, Kozawa O. Prostaglandin D<sub>2</sub> induces the phosphorylation of HSP27 in osteoblasts: function of the MAP kinase superfamily. Prostaglandins Leukot Essent Fatty Acids 75: 61-67, 2006.
18. Takai S, Tokuda H, Hanai Y, Kozawa O. Phosphatidylinositol 3-kinase/Akt plays a part in tumor necrosis factor- $\alpha$ -induced interleukin-6 synthesis in osteoblasts. Horm Metab Res 38: 563-569, 2006.
19. Hanai Y, Tokuda H, Yasuda E, Noda T, Ohta T, Takai S, Kozawa O. Up-regulation by Zinc of FGF-2-induced VEGF release through enhancing p44/p42 MAP kinase activation in osteoblasts. Life Sci 80: 230-234, 2006.
20. 長屋政博. 認知症に対する作業療法 Aging & Health 39:12-13, 2006.
21. Tanaka S, Nagaya M, et al. Comparison of rat mandible bone characteristics in F344 substrains, F344/Du and F344/N. Exp. Anim 55(5): 415-418, 2006.
22. 長屋政博. 脳血管障害のリハビリテーション 大内尉義編集: 高齢者への包括的アプローチとリハビリテーション メジカルビュー社 178-186, 2006.
23. 長屋政博. 介護予防にむけたリハビリテーション 未病のテキスト 金芳堂 187-190, 2006.
24. 長屋政博, 原田敦. 転倒予防 大内尉義編集: 高齢者の退院支援と在宅医療 メジカルビュー社 165-171, 2006.

25. 奥泉宏康、長屋政博、原田敦. 転倒予防のエビデンスと対策について教えてください 骨粗鬆症治療 5: 81-85, 2006.
26. 奥泉宏康、原田敦. 転倒・骨折の予防 リウマチ科 36: 204-210, 2006.
27. 奥泉宏康、原田敦. ビタミンDの骨密度・骨強度改善の効果 CLINICAL CALCIUM 16: 31-37, 2006.
28. 奥泉宏康、朴眩泰、小松泰喜、武藤芳照. ビタミンD研究の25年の歩み～転倒・筋力に関わる最新の話題 THE BONE 20: 95-100, 2006.
29. 斎藤拓也、加藤智香子. 高齢者における反応時間と転倒との関係について—動作部位・動作の種類に着目して— 名古屋大学医学部保健学科卒業論文集 1-4, 2007.
30. 中島由季、加藤智香子. 地域在住高齢者の足部の問題と関連因子の検討—バランス機能に着目して— 名古屋大学医学部保健学科卒業論文集 1-6, 2007.
31. Tokuda H, Takai S, Matsushima-Nishiwaki R, Akamatsu S, Hanai Y, Hosoi T, Harada A, Ohta T, Kozawa O. (-)-Epigallocatechin gallate enhances prostaglandin F<sub>2α</sub>-Induced VEGF synthesis Via Upregulating SAPK/JNK activation in osteoblasts. J Cell Biochem 100: 1146-1153, 2007.
32. Tokuda H, Takai S, Matsushima-Nishiwaki R, Akamatsu S, Hanai Y, Hosoi T, Harada A, Ohta T, Kozawa O. (-)-Epigallocatechin gallate suppresses endothelin-1-induced interleukin-6 synthesis in osteoblasts: Inhibition of p44/p42 MAP kinase activation. FEBS Letters 581: 1311-1316, 2007.
33. Tokuda H, Hanai Y, Matsushima-Nishiwaki R, Yamauchi J, Doi T, Harada A, Takai S, Kozawa O. Rho-kinase regulates endothelin-1-stimulated IL-6 synthesis via p38 MAP kinase in osteoblasts. Biochemical and Biophysical Research Communications. 362: 799-804, 2007.
34. Hayasaka K, Nihashi T, Matsuura T, Yagi T, Nakashima K, Kawabata Y, Ito K, Katoh T, Sakata K, Harada A. Metastasis of the gastrointestinal tract: FDG-PET imaging. Ann Nucl Med 21: 361-365, 2007.
35. Tokuda H, Takai S, Hanai Y, Harada A, Matsushima-Nishiwaki R, Akamatsu S, Ohta T, Kozawa O. Platelet-derived growth factor-BB amplifies PGF<sub>2α</sub>-stimulated VEGF synthesis in osteoblasts: Function of phosphatidylinositol 3-kinase. Prostaglandins Leukot Essent Fatty Acids. 77:187-193, 2007
36. Takai S, Tokuda H, Hanai Y, Harada A, Yasuda E, Matsushima-Nishiwaki R,

- Kato H, Ogura S, Ohta T, Kozawa O. Negative regulation by p70 S6 kinase of FGF-2-stimulated VEGF release through stress-activated protein kinase/c-Jun N-terminal kinase in osteoblasts. *J Bone Miner Res.* 22:337-346, 2007.
37. 原田敦. 運動器不安定症と今後の展開. 整形・災害外科 27-35, 2007.
38. 原田敦, 松井康素, 奥泉宏康, 竹村真里枝, 若尾典充, 長屋政博, 水野雅士. 転倒・骨折予防の立場からみた骨強度の評価. *Osteoporosis Jpn* 15: 152-154, 2007.
39. 竹村真里枝, 松井康素, 原田敦, 安藤富士子, 下方浩史. 地域在住中高年者の骨代謝マーカーによる骨量減少/骨粗鬆症予測. *Osteoporosis Jpn* 15: 28-32, 2007.
40. 加藤智香子, 猪田邦雄, 原田敦, 長屋政博, 徳田治彦. 施設入所高齢者の転倒恐怖とQOL, ADL, 身体活動量との関連. *Osteoporosis Japan* 317-319, 2007.
41. Takai S, Tokuda H, Hanai Y, Kozawa O. Limitation by p70 S6 kinase of PDGF-BB-induced IL-6 synthesis in osteoblast-like MC3T3-E1 cells. *Metabolism* 56: 476-483, 2007.
42. Takai S, Tokuda H, Hanai Y, Kozawa O. Activation of phosphatidylinositol 3-kinase/Akt limits FGF-2-induced VEGF release in osteoblasts. *Mol Cell Endocrinol.* 267:46-54, 2007.
43. Yamauchi J, Takai S, Matsushima N, Nishiwaki R, Hanai Y, Doi T, Kato H, Ogura S, Kato K, Tokuda H, Kozawa O. (-)-Epigallocatechin gallate inhibits prostaglandin D<sub>2</sub>-stimulated HSP27 induction via suppression of the p44/p42 MAP kinase pathway in osteoblasts. *Prostaglandins Leukot Essent Fatty Acids.* 77:173-179,2007.
44. 中澤信, 長屋政博. 疾患特有の評価法 パーキンソン病・総合リハビリテーション 35(1):55-60, 2007.
45. 長屋政博. 転倒予防教室の意義と今後の展望. *Calcitonin Osteoprosis* No7: 1-3, 2007.
46. 奥泉宏康. 転倒による骨折のバイオメカニクス. *身体教育医学研究*8: 75-77, 2007.
47. 奥泉宏康. ヒッププロテクターの現状と課題. *GERONTOLOGY NEW HORIZON* 19(3): 185-189, 2007.
48. 奥泉宏康, 武藤芳照. 人はなぜ転ぶのか? 落ちるのか? *Nursing Today* 22(12): 28-33, 2007.
49. 内藤善規, 加藤智香子. 地域在住高齢者の骨密度に関連する要因の検討. *名古屋大学医学部保健学科卒業論文集.* 1-6, 2008.

50. 川村皓生、加藤智香子. 地域在住高齢者と介護施設高齢者の健康関連QOLに関連する因子の検討. 名古屋大学医学部保健学科卒業論文集. 1-9, 2008.
51. Tokuda H, Takai S, Hanai Y, Harada A, Matsushima-Nishiwaki R, Kato H, Ogura S, Kozawa O. Potentiation by platelet-derived growth factor-BB of FGF-2-stimulated VEGF release in osteoblasts. *J Bone Miner Metab* 26: 335-341, 2008.
52. Tokuda H, Takai S, Hanai Y, Matsushima-Nishiwaki R, Yamauchi Y, Harada A, Hosoi T, Ohta T, O Kozawa. (-)-Epigallocatechin Gallate Inhibits Basic Fibroblast Growth Factor-stimulated Interleukin-6 Synthesis in Osteoblasts . *Horm Metab Res* 40: 674-678, 2008.
53. Kuno M, Takai S, Matsushima-Nishiwaki R, Minamitani C, Mizutani J, Otsuka T, Harada A, Adachi S, Kozawa O, Tokuda H. Rho-kinase inhibitors decrease TGF- $\beta$ -stimulated VEGF synthesis through stress-activated protein kinase/c-Jun N-terminal kinase in osteoblasts. *Biochemical pharmacology* 77(2): 196-203, 2009.
54. Kato C, Ida K, Kawamura M, Nagaya M, Tokuda H, Tamakoshi A, Harada A. Relation of falls efficacy scale (FES) to quality of life among nursing home female residents with comparatively intact cognitive function in Japan. *Nagoya J. Med. Sci.* 70: 19-27, 2008.
55. 原田敦、中野哲雄、倉都滋之、出口正男、末吉泰信、町田正文、伊東学. 高齢者脊椎骨折の入院治療に関する施設特性格全国調査 臨床整形外科 43(4) 303-308, 2008.
56. 加藤智香子、猪田邦雄、長屋政博、徳田治彦、奥泉宏康、原田敦. 介護施設女性高齢者の転倒自己効力感尺度 (Falls Efficacy Scale : FES) に関連する要因. 運動療法と物理療法 (印刷中)
57. 原田敦. ヒッププロテクターの骨折予防効果 日本医師会雑誌137 : 2286, 2009.
58. 原田敦、林泰史、寺本明、鈴木隆雄. 座談会 転倒・転落の原因から予防・治療まで 日本医師会雑誌 137 : 2235-2247, 2009.
59. 原田敦、岡本純明、三木隆己、岩本俊彦. 一般診療における高齢者骨粗鬆症の治療. *Geriat Med* 46(3): 905-917, 2008.
60. Takai S, Hanai Y, Matsushima-Nishiwaki R, Minamitani C, Otsuka T, Tokuda H, Kozawa O. p70 S6 kinase negatively regulates FGF-2-stimulated IL-6 synthesis

- in osteoblasts: function at a point downstream from protein kinase C. *J. Endocrinol.* 197: 131-137, 2008.
61. Hayashi K, Takai S, Matsushima-Nishiwaki R, Hanai Y, Kato K, Tokuda H, Kozawa O. (-)-Epigallocatechin gallate reduces transforming growth factor  $\beta$ -stimulated HSP27 induction through the suppression of stress-activated protein kinase/c-Jun N-terminal kinase in osteoblasts. *Life Sci.* 82: 1012-1017, 2008.
  62. Kato H, Takai S, Matsushima-Nishiwaki R, Adachi S, Minamitani C, Otsuka T, Tokuda H, Akamatsu S, Doi T, Ogura S, Kozawa O. HSP27 phosphorylation is correlated with ADP-induced platelet granule secretion. *Arch. Biochem. Biophys.* 475: 80-86, 2008.
  63. Minamitani C, Otsuka T, Takai S, Matsushima-Nishiwaki R, Adachi S, Hanai Y, Mizutani J, Tokuda H, Kozawa O. Involvement of rho-kinase in prostaglandin F<sub>2a</sub>-stimulated interleukin-6 synthesis via p38 mitogen-activated protein kinase in osteoblasts. *Mol. Cell. Endocrinol.* 291: 27-32, 2008.
  64. Minamitani C, Takai S, Matsushima-Nishiwaki R, Hanai Y, Otsuka T, Kozawa O, Tokuda H. Raloxifene-induced acceleration of platelet aggregation. *Intern. Med.* 47: 1523-1528, 2008.
  65. Tokuda H, Takai S, Matsushima-Nishiwaki R, Hanai Y, Adachi S, Minamitani C, Mizutani J, Otsuka T, Kozawa O. Function of Rho-kinase in prostaglandin D<sub>2</sub>-induced interleukin-6 synthesis in osteoblasts. *Prostaglandins Leukot. Fatty Acids.* 79: 41-46, 2008.
  66. Yamauchi J, Takai S, Matsushima-Nishiwaki R, Adachi S, Minamitani C, Natsume H, Mizutani J, Otsuka T, Takeda J, Harada A, Kozawa O, Tokuda H. Tacrolimus but not cyclosporine A enhances FGF-2-induced VEGF release in osteoblasts. *Intern. J. Mol. Med.* 23: 267-272, 2009.
  67. Sumi Y, Miura H, Nagaya M, et al. Relationship between oral function and general condition among Japanese nursing home residents. *Archives of gerontology and Geriatrics* 48: 100-105, 2009.
  68. 田中慎、長屋政博、他. 実験動物の大腿骨. 九州実験動物雑誌 24: 3-8, 2008.
  69. 長屋政博、中澤信. 疾患別VF・VEのみかたパーキンソン症候群. *Journal of Clinical Rehabilitation* 17: 479-484, 2008.

70. 長屋政博. 高齢者の介護とリハビリテーション 大内尉義編：実地医科のための高齢者診療ガイド 139-145, 同人社 初版 2008.
71. 原田敦、長屋政博. 歩行障害 大内尉義編：実地医科のための高齢者診療ガイド 58-61, 同人社 初版 2008.
72. 奥泉宏康、原田敦. 高齢者医療における骨粗鬆症と骨折予防 関節外科 27: 781-87, 2008.
73. 奥泉宏康、原田敦. 骨・軟骨疾患の予防・治療の現状と将来 ②運動（ヒッププロテクターなどの装具を含む） THE BONE 22:387-89, 2008.
74. 奥泉宏康. ビタミンDと転倒. 骨粗鬆症治療 7: 196-202, 2008.
75. 奥泉宏康、原田敦. 転倒・骨折のバイオメカニクス. CLINICAL CALCIUM 18: 754-60, 2008.
76. 奥泉宏康. 後期高齢者によくみられる症状とプロブレム 転倒・骨折-実態と予防 - medicina 45: 1226-29, 2008.
77. 奥泉宏康. 転倒予防に対するリハビリテーション-ヒッププロテクターによる骨折予防を含む- The BONE 22: 499-502, 2008.
78. 吉水久恵、加藤智香子. Single task ジャンプ反応時間・Dual task ジャンプ反応時間の加齢変化と地域在住高齢者における転倒歴との関連. 名古屋大学医学部保健学科卒業論文集 1-7, 2009.
79. 今宿万里江、加藤智香子. 高齢者における側方バランスと転倒の関連～前方バランスと比較して～ 名古屋大学医学部保健学科卒業論文集 1-9, 2009.





## 研究成果の刊行物・別刷

## Can you diagnose for vertebral fracture correctly by plain X-ray?

Z. Ito · A. Harada · Y. Matsui · M. Takemura ·  
N. Wakao · T. Suzuki · T. Nihashi · S. Kawatsu ·  
H. Shimokata · N. Ishiguro

Received: 31 August 2005 / Accepted: 20 March 2006 / Published online: 18 August 2006  
© International Osteoporosis Foundation and National Osteoporosis Foundation 2006

**Abstract** *Introduction:* A wrong diagnosis of latent vertebral fracture is often made when it is based on plain X-ray imaging. Magnetic resonance imaging (MRI) has a high degree of accuracy for the definite diagnosis. This study was designed to identify ways to support improvements in the diagnostic accuracy of plain X-ray (X-P). *Methods:* We studied X-P and MRI images of 120 women and men (age range: 50–96 years). Five orthopedists and two radiologists interpreted front and lateral thoracolumbar X-Ps and MRI images. The correct diagnosis rate for the presence and location of incident vertebral fractures and the correct diagnosis rate according to morphological classifications were analyzed. *Results:* A correct diagnosis of incident fractures was made in 51.5% of cases overall. Diagnoses of non-incident fracture based on X-P in those cases with incident fracture based on MRI (false positive) occurred in 24.8% of the patients, while diagnoses of incident fracture based on X-P in those cases without incident fracture based on MRI (false

negative) occurred in 6.5% of the patients. The application of morphological classifications (the primary osteoporosis diagnostic criteria and Yoshida's classification) resulted in the correct diagnosis rate being significantly higher in the group without prevalent fracture even when there were morphological changes (wedge, indented, protruding type) in the anterior bone cortex. Odds ratios were investigated for factors that would affect the correct diagnosis rate, including age, body weight, lumbar vertebrae bone mineral density, and examiner ability. In an overall investigation, age (OR=0.660), body weight (OR=2.082), and examiner ability ( $p=0.0205$ ) affected the correct diagnosis rate. *Conclusion:* The correct diagnosis rate for incident vertebral fractures with X-Ps was low (24.8%) and in cases with prevalent fractures, the rate was even lower (16.8%), but the number of prevalent fractures and BMD did not exert an effect. One key improving the correct diagnosis rate may be to pay attention to morphological changes in the anterior bone cortex.

Z. Ito (✉) · A. Harada · Y. Matsui · M. Takemura · N. Wakao ·  
T. Suzuki

Department of Orthopedic Surgery,  
National Center for Geriatrics and Gerontology,  
36-3 Gengo Morioka-cho,  
Obu, Japan  
e-mail: z.ito@med.nagoya-u.ac.jp  
Tel.: +81-562-462311  
Fax: +81-562-482373

T. Nihashi · S. Kawatsu  
Department of Radiology,  
National Center for Geriatrics and Gerontology,  
36-3 Gengo Morioka-cho,  
Obu, Japan

H. Shimokata  
Department of Epidemiology,  
National Institute for Longevity Sciences,  
Aichi, Japan

N. Ishiguro  
Department of Orthopedic Surgery,  
Nagoya University,  
Nagoya, Japan

**Keywords** Anterior bone cortex · Bone mineral density ·  
Diagnosis rate · Latent fractures · Spinal fragility fractures

### Introduction

Elderly outpatients with complaints of severe lumbar back pain in almost all cases undergo plain X-ray (X-P), from which a diagnosis of the underlying condition should be made. At such times an existing lesion of vertebral disk degeneration or osteoporosis can often conceal a latent incident spinal fracture, with the result that a delayed diagnosis can make it difficult to prevent post-fracture sequelae or other problems [1]. However, reports are occasionally received that an accurate diagnosis of the existence or location of the incident fracture is difficult with X-P images only and that X-P screening images are not effective for low back pain [2, 3]. Meanwhile, many reports have stated that magnetic resonance imaging (MRI) has a high degree of accuracy for the definite diagnosis of incident spinal fracture, and it continues to be used as the

more useful tool [4-6]. However, due to limitations in equipment and considerations that must be given to the economics of medical treatments, it is not possible to use MRI with all patients. In the present study, therefore, with diagnosis by MRI taken to be the correct diagnosis, we conducted a multi-lateral analysis of the diagnostic accuracy of several orthopedic surgeons and radiologists who based their diagnoses on X-P images, in order to identify ways to support improvements in diagnostic accuracy. This is a cross-sectional study.

## Materials & methods

### Participants

The subjects were patients above the age of 50 who were examined at the authors' hospitals between May 1999 and January 2004, and who had undergone MRI within 4 weeks of the initial examination. A non-incident fracture group consisted of patients without incident vertebral fractures, while an incident fracture group consisted of patients with incident vertebral fragility fractures caused by weak external force, such as that sustained in falls from a standing position. One hundred twenty-three patients had these conditions. After excluding patients who had a history of primary or metastatic bone tumor, infectious disease, hematological disorders, or compression fracture within the previous year, which would leave spots with high signal intensity on the MRI images (three patients), the final number of subjects for the study was 120, of whom 112 were women and eight were men, with ages ranging from 50 to 96 years (mean age: 75.6 years).

### Measurements

Five orthopedists and two radiologists from our hospital interpreted anteroposterior (A-P) and lateral thoracolumbar X-Ps taken during the initial examination. They did not question the patients or have access to physiological

findings, and the images were arranged by a third party with the patients' IDs and names concealed. The correct diagnoses were taken to be those of two radiologists not involved in the treatment of the patients who, in consultation with each other, reached the same conclusion based on MRI [1.5T, T1-weighted images (SE: TR/TE = 400/15 ms); T2-weighted images (SE: TR/TE = 2500/120 ms)]. In this study, a definition of a fracture based on the MRI image also included a bone bruise without deformity as an incident fracture. Differences in the ability of the five orthopedists to interpret spinal X-P images were investigated in advance. The subjects of this investigation were 89 healthy community residents who underwent thoracolumbar spine X-P for the purpose of a long-term longitudinal epidemiological study at out hospital. Each orthopedist classified the vertebral spines (Nathan's classification [7]) on an A-P thoracolumbar image, after which intraclass correlation coefficients were calculated using SAS (Statistical Analysis Software, Cary N.C.) ver. 8.2, and the level of coincidence was observed. The results revealed no significant difference in the ability of the orthopedists to interpret radiographs, with intra-class correlation (ICC) = 0.739 [95%CI for ICC: 0.679-0.799]. Accordingly, assuming that there was no difference in the ability to interpret spinal X-P images, the correct diagnosis rate for the presence and location of incident spinal fractures and the correct diagnosis rate according to the morphological classifications (classifications of Genant et al. [8] and Yoshida [9]) of the incidental fractured vertebral body were analyzed, and subjects were divided into three groups for the analysis of factors affecting correct diagnosis: (1) non-incident fracture group with and without prevalent fractures (non-incident fracture group); (2) incident fracture group without prevalent fractures; (3) incident fracture group with prevalent fractures. Bone mineral density (BMD) was measured using dual energy x-ray absorptiometry (DPX; Lunar, GE Healthcare, UK) in bones of the entire body, the lumbar vertebrae, and the femoral neck. The density for the lumbar vertebrae (L2-4) was adopted for the present study.

Table 1 Baseline data (means  $\pm$  standard deviation)

l	Fracture group	Incident fracture group		Non-incident fracture group <sup>a</sup>	
		Without prevalent fracture	With prevalent fracture		
*Number	67	24	43	53	
Age (year)	79.9 $\pm$ 7.9	76.8 $\pm$ 7.2	81.1 $\pm$ 7.9	68.9 $\pm$ 9.6	
Weight (kg)	43.4 $\pm$ 8.3	46.1 $\pm$ 9.1	42.2 $\pm$ 7.7	49.9 $\pm$ 7.3	
Height (cm)	146.3 $\pm$ 7.1	148.1 $\pm$ 5.5	145.5 $\pm$ 7.6	148.39 $\pm$ 6.2	
Lumbar BMD(g/cm <sup>2</sup> )	0.74 $\pm$ 0.19	0.84 $\pm$ 0.18	0.70 $\pm$ 0.27	0.90 $\pm$ 0.24	
One new fracture	50	21	29	-	
Two new fractures	9	2	7	-	<i>p</i> <0.0001
Three new fractures	7	1	6	-	
More new fractures	1	0	1	-	

Values are mean $\pm$ SD

<sup>a</sup>Significant differences were seen in age, height, weight, and lumbar vertebrae BMD

## Statistical analysis

SAS ver. 8.2 was used for the accumulation and analysis of data. In comparing the correct diagnosis rate for fractured vertebral body morphology, adjustments were made using the Cochran-Mantel-Haenszel method for variations in age, body weight, lumbar spine bone mineral density, and examiner ability, and analysis was conducted with ANOVA, Tukey's multiple comparison test, and logistic regression analysis.

## Results

### Number of patients and fractured vertebrae

Of the 120 patients, 67 patients were diagnosed with incident fractures with and without prevalent fractures in 95 vertebrae, including single incident fractures in 50 patients and two or more incident fractures in 17 patients. There was non-incident fracture with and without prevalent fractures in 53 patients. The group of incident fractures without prevalent fractures consisted of 24 patients and 28 vertebrae, and with prevalent fractures, of 43 patients and 67 vertebrae. Significant differences were seen in age, height, weight, and lumbar vertebrae BMD ( $p < 0.0001$ ) (Table 1).

### A breakdown of correct and incorrect diagnoses

A correct diagnosis of incident fracture was made in 51.5% of cases overall. A breakdown shows that in cases when non-incident fracture was seen by MRI the correct response of non-incident fracture (true negative) was made in 37.7% of cases and the correct diagnosis of incident fracture (true positive) was judged to have occurred in 13.8% of cases. The location of incident fracture was mistaken in 17.2% of the cases. Responses of non-incident fracture on X-P images in cases with incident fracture (false negative) occurred in 24.8% of the cases, while responses of incident fracture on X-P images in cases of non-incident fracture (false positive) occurred in 6.5% of the cases (Table 2).

### The overall rate of correct diagnosis

#### Non-incident fracture group

We next compared the correct diagnosis rate of incident fractures by the five examiners in each of the three groups. The correct diagnosis rate of the five examiners was high overall, reaching 85.3% (73.6–92.5%) in the non-incident fracture group. The overall diagnosis rate was also high with no significant variation between the five examiners ( $p = 0.486$ ).

#### Incident fracture group without prevalent fractures

The overall correct diagnosis rate for the incident fracture group without prevalent fractures was 39.3% (21–58.3%), and significant variation was seen between the five examiners ( $p = 0.04$ ).

#### Incident fracture group with prevalent fractures

Despite the low overall correct diagnosis rate of 16.8% (9.3–21%) in the incident fracture group with prevalent fractures, no significant difference was seen in the correct diagnosis rate between the five examiners, and overall the diagnosis rate was low ( $p = 0.432$ ).

Thus, the correct diagnosis rate for incident fractures decreased significantly in the non-incident fracture group followed by the incident fracture group without prevalent fractures, and the incident fracture group with prevalent fractures, in that order. However, a second investigation after adjusting for differences in age, weight, and lumbar vertebrae BMD revealed significant variation in all three groups (Fig. 1).

#### The kappa score of interexaminers

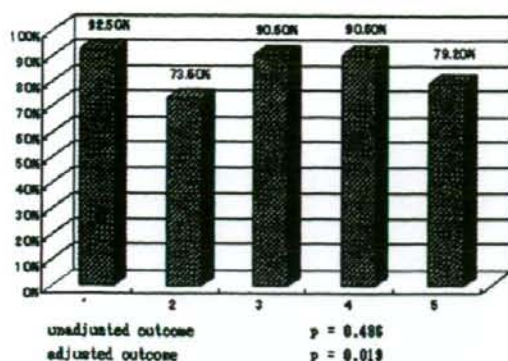
The median kappa-score of all examiners was 0.65 [0.51 (min.) to 0.81 (max.)]. The median kappa-score of inter-orthopedists was 0.65 (0.51–0.72), while the kappa-score of inter-radiologists was 0.69. The median kappa-score of orthopedists-radiologists was 0.63 (0.54–0.81) (Fig. 1).

Table 2 A breakdown of correct and incorrect diagnoses\*

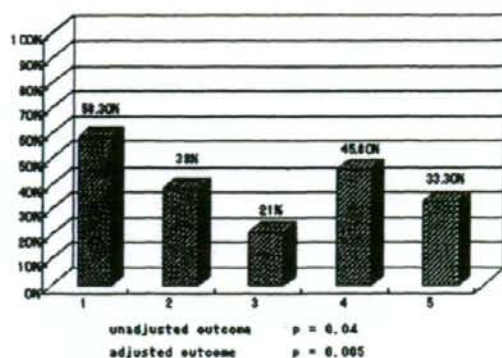
	Fracture - (MRI)	Fracture +	Total		Diagnosis rate
Fracture-(X-P)	37.68%	24.83%	62.51%	→	Fx-/Fx-: 37.68%
Fracture +	6.49%	31%	37.495%		Fx+/Fx+: 13.83%
		(Correct: 13.83%, level mistake: 17.17%)			
Total	44.17%	55.83%	100%		Total: 51.51%

\*Fracture with a -/+ (MRI) means the correct diagnosis; fracture with a -/+ (X-P) means the examiners' answers

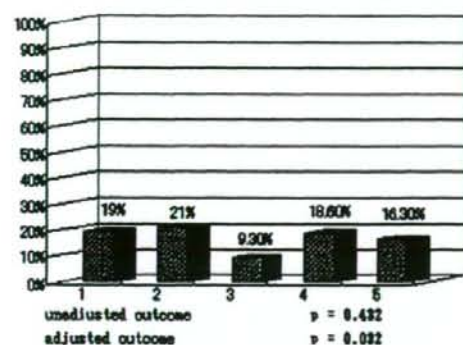
A non incident fracture group



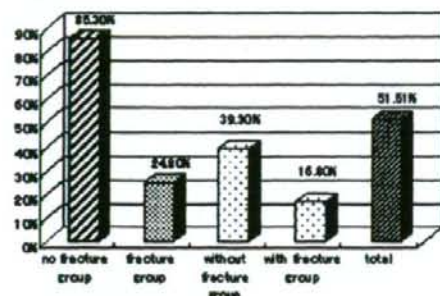
B incident fracture group without prevalent fractures



C incident fracture group with prevalent fractures



D Average



E

	Total	inter-orthopedists	inter-radiologists	orthopedists-radiologists
K score: median	0.85	0.85	0.83	0.83
(min-max)	(0.51-0.81)	(0.51-0.72)	—	(0.55-0.81)

Fig. 1 Diagnosis rate by the five examiners. a Significant variation was seen in the non-incident fracture group after adjustment. b Significant variation was seen in the incident fracture group without prevalent fractures. c Significant variation was seen in

the incident fracture group with prevalent fractures after adjustment. d Average of diagnosis rate. e The kappa score of interexaminers. These results were moderate

The rate of correct diagnosis based on the number of prevalent fractures

The next variable investigated was the correct diagnosis rate by number of prevalent fractures in the incident fracture group with prevalent fractures. No correlation was found between the correct diagnosis rate and the number of complicating prevalent fractures when the subjects were divided into either six groups according to the number of prevalent fractures (one fracture to six or more fractures) or two groups (one fracture vs. two or more fractures) ( $p=0.139, 0.284$ , respectively; Fig. 2).

The rate of correct diagnosis by morphological classification

#### The primary osteoporosis diagnostic criteria

We then looked at the correct diagnosis rate for incident fractures by morphological classification of the vertebral body in the incident fracture groups with and without prevalent fractures. The morphological classifications used were the primary osteoporosis diagnostic criteria of Genant et al. [8] and Yoshida's classification [9] (Fig. 3). Using the primary osteoporosis diagnostic criteria of Genant, the correct diagnosis rate was high for wedge-type fractures in the combined results for the incident fracture groups with and without prevalent fractures (fracture group)

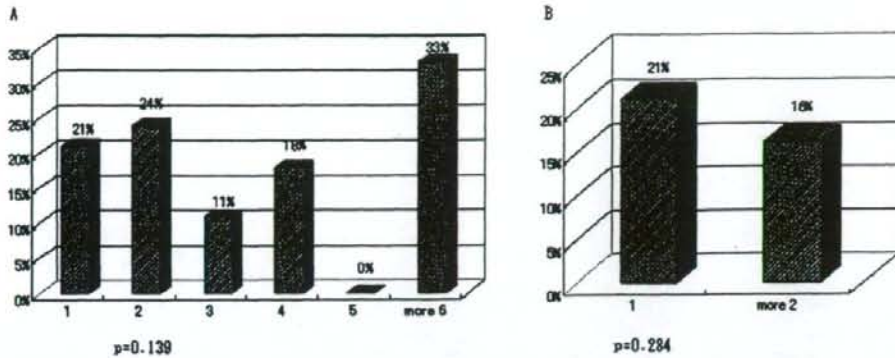


Fig. 2 No correlation was found between correct diagnosis rate and the number of complicating prevalent fractures. a Diagnosis rate when divided into one of six groups. b Diagnosis rate when divided into one of two groups

( $p<0.0001$ ). Similar results were obtained even after adjustment had been made for variation between the examiners. However, this significant difference disappeared after age, body weight, and lumbar BMD had been adjusted for. The same results were obtained in the incident fracture group with prevalent fractures, but in this case a significant difference was seen after correction in the incident fracture group without prevalent fractures ( $p=0.0455$ ) (Table 3).

#### Yoshida's classification

When Yoshida's classification was applied, the correct diagnosis rate was high for intended and protruding types of fractures ( $p<0.0001$ ). The correct diagnosis rate was significantly higher in the incident fracture group without prevalent fractures even when there were morphological changes (wedge, intended and protruding type) in the anterior bone cortex. Conversely, the correct diagnosis rate was low in the incident fracture group with prevalent fractures, end plate compression and slippage type fractures with no morphological changes in the anterior bone cortex, and in "miscellaneous" cases that belonged to no category and had almost no morphological change.

#### The primary osteoporosis diagnostic criteria



#### Yoshida's classification

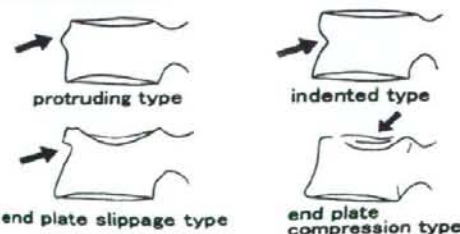


Fig. 3 The morphological classifications used were the primary osteoporosis diagnostic criteria of Genant [8] and Yoshida's [9] classification. Yoshida's criteria is for incident fractures and classified in four types as follows: protruding type, the anterior bone cortex disrupted protrudes anteriorly; indented type, the anterior bone cortex disrupted indents posteriorly; end plate slippage type, the anterior edge of the end plate disrupted displaces anteriorly; end plate compression type, the center of the end plate disrupted indents and depressed

#### Odds ratios affected the rate of correct diagnosis

Odds ratios (ORs) were investigated for factors that would affect the correct diagnosis rate, including age, body weight, lumbar vertebrae BMD, and examiner ability. In an overall investigation, age (OR=0.660), body weight (OR=2.082), and examiner ability ( $p=0.0205$ ) affected the correct diagnosis rate. A younger age and greater body weight resulted in higher correct diagnosis rates, and results were also affected by the examiner's ability. None of these factors had an effect in the non-incident fracture group. Significant variation is seen in examiner's ability in Fig. 1, but not to the extent that results were affected ( $p=0.0709$ ). In the fracture groups, both body weight (OR=2.206) and examiner ability ( $p=0.0039$ ) affected the results. This was also seen in the incident fracture group without prevalent fractures alone, but in the incident fracture group with prevalent fractures alone only lumbar BMD had an effect (OR=1.574) (Table 4).

#### Discussion

The prevalence rate of spinal fracture is thought to be 117 people per 100,000 in the population [10], and the lifetime

**Table 3** Diagnosis rate<sup>a</sup> according to the morphological classifications

Genant classification							
Fracture type	Numbers	Diagnosis rate – total fracture group	Numbers	Diagnosis rate – without prevalent fractures	Numbers	Diagnosis rate without prevalent fractures	
Wedge	22	40.90%	6	63.30%	16	32.50%	
Crush	9	26.70%	3	53.30%	6	13.30%	
Biconcave	17	24.70%	4	40.00%	13	20.00%	
Other	40	18%	12	30%	28	12.80%	
a <sup>b</sup>	<i>p</i> <0.0001		<i>p</i> =0.0011		<i>p</i> <0.0011		
b	<i>p</i> <0.0001						
c	<i>p</i> =0.9123		<i>p</i> =0.0455		<i>p</i> =0.9516		
Yoshida's classification							
Fracture type	Numbers	Diagnosis rate – total fracture group	Numbers	Diagnosis rate – without prevalent fractures	Numbers	Diagnosis rate without prevalent fractures	
End plate slip-page	17	29.40%	7	45.71%	10	18.00%	
Intended protruding	8	46.70%	2	90.00%	6	40.00%	
End plate compression	9	60%	4	80.00%	5	44.00%	
Other	6	10%	2	10%	4	10.00%	
a <sup>b</sup>	<i>p</i> <0.0001		<i>p</i> =0.0016		<i>p</i> =0.0173		
b	<i>p</i> <0.0001						
c	<i>p</i> =0.4708		<i>p</i> =0.0455		<i>p</i> =0.6953		

<sup>a</sup>The correct diagnosis rate was higher in the incident fracture group without prevalent fractures even when there were morphological changes in the anterior bone cortex. In seven cases, we were unable to classify the morphology because of indistinctness

<sup>b</sup>a, Unadjusted *p* value; b, *p* value adjusted with examiners; c *p* value adjusted with age, weight, BMD and examiners

risk of spinal fracture in women over the age of 50 rises to about 40% [11]. Vertebral body fractures result in pain and functional restrictions, and provoke a marked decrease in quality of life [12, 13]. Therefore, early prevention of spinal fractures and accurate diagnosis and treatment are crucial. There are various reports on the diagnosis of incident spinal fracture [14], but a diagnostic gold standard has yet to be established. Nearly all institutions first take X-P images for patients presenting with lumbar pain. However, it is difficult to determine from X-P images the presence and location of incident fragility fractures in elderly patients with osteoporosis at the time of injury; it is even more difficult when the patient has prevalent fractures. Furthermore, incident fractures are defined as those vertebral bodies that show distinct morphologic changes or osteosclerosis change on the follow-up X-P

images. Consequently, we usually cannot detect incident fractures at the early stage of diagnosis.

With respect to the effectiveness of X-Ps for lumbar pain disease in general, David et al. reported that 17.8% of patients in an emergency department received unnecessary lumbar X-Ps [15], while Khoo et al. reported that 90.5% of AP views on X-Ps have no benefit and were effective only in assessing the sacroiliac joint [16]. Thus, establishing a diagnosis for lumbar pain is difficult with X-P alone, and most cases require MRI. Many reports attest to the high diagnostic accuracy of MRI, and it continues to be more useful tool in diagnosing spinal fracture [4–6]. In MRI images, fractures are defined so that an acute fracture associated with hemorrhage and edema increases the focal water content and thus increases the signal on T2-images. With an osteoporotic fracture, the hemorrhage will be organized and the edema will decrease, giving a low to

**Table 4** Odds ratios of factors that would affect the correct diagnosis rate

Factors	Total		Non-incident fracture group		Total fracture group		Without prevalent fractures		With prevalent fractures	
	Odds ratio	<i>p</i> value	Odds ratio	<i>p</i> value	Odds ratio	<i>p</i> value	Odds ratio	<i>p</i> value	Odds ratio	<i>p</i> value
Age	0.66	<0.001	0.781	0.2817	1.053	0.7098	1.02	0.9291	1.254	0.1966
Body weight	2.082	<0.001	0.661	0.0876	2.206	<0.001	3.002	<0.0001	1.42	0.1303
Lumbar BMD	1.246	0.072	1.108	0.676	1.043	0.7873	0.65	0.0584	1.574	0.0478
Ability of the examiner	-	0.0205	-	0.0709	-	0.0039	-	0.0349	-	0.1163

Results were affected by examiner ability, age and body weight

intermediate signal intensity on T2-weighted images. It has already been reported that femoral neck fractures cannot be judged on X-P images and that MRI diagnosis is useful in cases of occult fracture. Pandey et al. reported that fractures are not discovered on X-P images and that even on MRI images, 30% show no fracture [17], while Rizzo et al. reported that occult fractures were detected on MRI in 36 of 62 patients (58%) [18].

With respect to spinal disease as well, Nakano et al. investigated the diagnostic accuracy of MRI for incident vertebral fractures. They took vertebral bodies showing signs of crush and bone sclerosis on follow-up X-P images to indicate true incident fractures and reported that the diagnostic sensitivity and specificity of MRI were 99.0% and 98.7%, respectively [19, 20]. They also reported that based on diagnosis with MRI it was possible to diagnose with precision a fracture in the early period of onset. In addition, Kanchiku et al. reported that the diagnostic rate of the fractured vertebral body was 98% by MRI, which was higher than the 87% for plain radiography ( $p=0.006$ ); in patients for whom no posterior wall injury was seen on X-P imaging at the time of the injury, intraspinal protrusion of the posterior wall of the vertebral body was diagnosed in 37% using MRI [21]. Eugene et al. reported that twice as many spinal diseases were detected when using MRI as when diagnosis was made from X-P imaging [2]. Thus, MRI is considered to be reliable in the diagnosis of incident fragility fracture. However, this high diagnostic accuracy also gives rise to some problems. Rupp et al. reported that in distinguishing between tumor and compression fracture on MRI images, compression fracture can only be diagnosed in those patients that have completely maintained normal marrow within the vertebrae and that it is difficult to make a distinction, due to changes in contrast effect and intensity, over multiple vertebrae or invasion to the posterior vertebral body wall [22]. In addition, Cuenod et al. reported that at 2 months after a spinal fracture is sustained, changes in brightness on MRI images have completely returned to normal in only 13% of the cases [23], indicating the possibility that old fractures can be mistaken for incident fractures. Equipment limitations at some institutions and economic problems make it impossible to conduct MRI with all patients. Jeffrey et al. compared MRI in the acute phase of lumbar pain with X-P over the clinical course and concluded that no cost benefit was achieved [24]. Thus, several problems are also encountered with the use of MRI in diagnosis.

Based on all of the points raised above, we re-examined X-P diagnosis and investigated whether the correct diagnosis rate with X-P in the initial examination could be improved. To our knowledge, this type of comparison has not been carried out to date, however, a search of the literature has revealed that various data sets are available on diagnosis rates for incident fractures with X-P. In a comparison of local and central readings, Pierre et al. reported a correct diagnosis rate of 95% in the non-fracture group and 66% in the fracture group [25]. Hachiya et al. reported a correct diagnosis rate of 43%, false positives in 41% of the cases, and false negatives in 16% [26]. Nakano

et al. reported a correct diagnosis rate of 51.5% [27], while Kanchiku et al. reported a high correct diagnosis rate of 87% [21]. However, factors such as unspecified measurement conditions, a small number of examiners, or non-uniform skill levels of examiners in these studies make them inadequate for the establishment of a correct diagnosis rate.

In the present study, a strict diagnosis was made together with radiologists, the ability of five orthopedists to interpret X-Ps was determined in advance to be uniform, and three groups were compared. The results of this analysis showed the correct diagnosis rate to be 51.5%, which did not differ greatly from the reports of previous investigators. However, the mean correct diagnosis rate for incident vertebral fracture group was 24.8%, and it was even lower – 16.8% – in the group with prevalent fractures. The correct diagnosis rate decreased in order of non-incident fracture group (highest), the incident fracture group without prevalent fractures, and the incident fracture group with prevalent fractures (lowest), a result which demonstrates anew the difficulty of diagnosing the location of fractures in the daily clinical setting. Moreover, after correcting for various factors, we found that there was a significant inter-examiner variation in all groups. This seems to indicate that the ability of an examiner to interpret radiographs is reflected in the correct diagnosis rate. In an examination based on the number of prevalent fractures, the correct diagnosis rate did not drop as the number of prevalent fractures increased, and no correlation was found. This finding that the number of prevalent fractures does not exert an effect is intriguing. Thus, even with prevalent fractures over multiple vertebrae, it is assumed that with diligence, incident fractures can be detected.

The previously mentioned criteria of Genant et al. were used in the analysis by morphological classification [8]. These criteria are commonly used in the diagnosis of osteoporotic vertebral body fractures. However, 45.5% of the cases in our study did not fit any type in these classifications, bringing some doubt to the judgments that have been made to date. We therefore conducted the investigation using these criteria in conjunction with Yoshida's classifications [9]. A high correct diagnosis rate was obtained for wedge type fractures with the diagnostic criteria for primary osteoporosis, and for protruding and indented type fractures with Yoshida's criteria; however, the correct diagnosis rate was low with the remaining types of fractures. Thus, a key to raising the correct diagnosis rate for incident fragility fractures may be to focus sufficient attention on morphological changes in the anterior bone cortex when diagnosing from X-P images.

In this investigation of factors influencing the correct diagnosis rate of osteoporotic vertebral body fractures, we found age, body weight, and examiner ability had an overall effect. The negative correlation seen with age, in which the correct diagnosis rate decreased as age increased, and the decrease in the correct diagnosis rate with lower body weight are understandable, but the finding that BMD did not exert an effect was intriguing. Moreover, the



finding that the ability of the examiner to interpret radiographs was reflected in the correct diagnosis rate indicates the importance of continuing efforts to improve ability.

Several points remain for future study, including the facts that the present study was a retrospective study and that the diagnosis was made without questioning the patients or pathological findings. Based on the results presented here, an investigation of how repeat readings will change the correct diagnosis rate should also be made. In any case, the finding that the correct diagnosis rate was low, even when made by orthopedists experienced in reading radiographs, is a finding that should be taken into consideration in the normal diagnosis of incident spinal fragility fractures with X-Ps only, and may be important in identifying keys for the development of new diagnostic criteria and more accurate diagnoses. The present study indicates the importance of not only improving the ability of examiners to interpret radiographs but also of the attention that should be paid to morphological changes in the anterior bone cortex during examinations.

**Acknowledgements** The authors wish to thank all the technicians who performed the measurements in the different centers.

## References

- Majumdar SR, Kim N, Colman I, Chahal AM, Raymond G, Jen H, Siminoski KG, Hanley DA, Rowe BH (2005) Incidental vertebral fractures discovered with chest radiography in the emergency department: prevalence, recognition, and osteoporosis management in a cohort of elderly patients. *Arch Intern Med* 165:905-909
- Gibson ES, Martin RH, Terry CW (1980) Incidence of low back pain and pre-placement x-ray screening. *J Occup Med* 22:515-519
- Simmons ED, Guyer RD, Graham-Smith A, Herzog R (2003) Radiograph assessment for patients with low back pain. *Spine J* 3:3S-5S
- Rankine JJ, Gill KP, Hutchinson CE, Ross ER, Williamson JB (1998) The therapeutic impact of lumbar spine MRI on patients with low back and leg pain. *Clin Radiol* 53:688-693
- McNally EG, Wilson DJ, Ostlere SJ (2001) Limited magnetic resonance imaging in low back pain instead of plain radiographs: experience with first 1000 cases. *Clin Radiol* 56: 922-925
- Shih TT, Tsuang YH, Huang KM, Chen PQ, Su CT (1996) Magnetic resonance imaging of vertebral compression fractures. *J Formos Med Assoc* 95:313-319
- Nathan H (1962) Osteophytes of the vertebral column. An anatomical study of their development according to age, race, and sex with consideration as to their etiology and significance. *J Bone Joint Surg* 44-A:243-268
- Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 8:1137-1148
- Yoshida T, Nanba H, Mimatsu K, Kasai T (2000) Treatment of osteoporotic spinal compression fractures. Conservative therapy and its limitation (in Japanese). *Clin Calcium* 10:53-58
- Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ 3rd (1992) Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. *J Bone Miner Res* 7:221-227
- Fujiwara S (2004) Degeneration of lumbar spine and QOL (in Japanese). *Ther Osteoporos* 3:32-37
- Nevitt MC, Ettinger B, Black DM, Stone K, Jamal SA, Ensrud K, Segal M, Genant HK, Cummings SR (1998) The association of radiographically detected vertebral fractures with back pain and function: a prospective study. *Ann Intern Med* 128:793-800
- O'Neill TW, Cockerill W, Matthis C, Raspe HH, Lunt M, Cooper C, Banzer D, Cannata JB, Naves M, Felsch B, Feisenberg D, Janott J, Johnell O, Kanis JA, Kragl G, Lopes Vaz A, Lyritis G, Masaryk P, Poor G, Reid DM, Reisinger W, Scheidt-Nave C, Stepan JJ, Todd CJ, Woolf AD, Reeve J, Silman AJ (2004) Back pain, disability, and radiographic vertebral fracture in European women: a prospective study. *Osteoporos Int* 15:760-765
- Ross PD, Davis JW, Epstein RS, Wasnich RD (1992) Ability of vertebral dimensions from a single radiograph to identify fractures. *Calcif Tissue Int* 51:95-99
- Isaacs DM, Marinac J, Sun C (2004) Radiograph use in low back pain: a United States Emergency Department database analysis. *J Emerg Med* 26:37-45
- Khoo LA, Heron C, Patel U, Given-Wilson R, Grundy A, Khaw KT, Dundas D (2003) The diagnostic contribution of the frontal lumbar spine radiograph in community referred low back pain-a prospective study of 1030 patients. *Clin Radiol* 58:606-609
- Pandey R, McNally E, Ali A, Bulstrode C (1998) The role of MRI in the diagnosis of occult hip fractures. *Injury* 29:61-63
- Rizzo PF, Gould ES, Lyden JP, Asnis SE (1993) Diagnosis of occult fractures about the hip. Magnetic resonance imaging compared with bone-scanning. *J Bone Joint Surg Am* 75: 395-401
- Nakano T, Inaba D, Takada K, Tsurugami H (2003) Rate of correct diagnosis for vertebral fracture by MRI and natural history (in Japanese). *Osteoporos Jpn* 11:25-28
- Nakano T, Ochi R, Miyazono K, Inaba D, Tsurugami H (2004) Diagnosis precision of MRI for fresh osteoporotic vertebral body fracture and a diagnosis by follow-up roentgenogram (in Japanese). *Osteoporos Jpn* 12:89-90
- Kanchiku T, Taguchi T, Kawai S (2003) Magnetic resonance imaging diagnosis and new classification of the osteoporotic vertebral fracture. *J Orthop Sci* 8:463-466
- Rupp RE, Ebraheim NA, Coombs RJ (1995) Magnetic resonance imaging differentiation of compression spine fractures or vertebral lesions caused by osteoporosis or tumor. *Spine* 20:2499-2503
- Cuenod CA, Laredo JD, Chevret S, Hamze B, Naouri JF, Chapaux X, Bondeville JM, Tubiana JM (1996) Acute vertebral collapse due to osteoporosis or malignancy: appearance on unenhanced and gadolinium-enhanced MR images. *Radiology* 199:541-549
- Jarvik JG, Hollingworth W, Martin B, Emerson SS, Gray DT, Overman S, Robinson D, Staiger T, Wessbecher F, Sullivan SD, Kreuter W, Deyo RA (2003) Rapid magnetic resonance imaging vs radiographs for patients with low back pain: a randomized controlled trial. *JAMA* 289:2810-2818
- Delmas PD, van de Langerijt L, Watts NB, Eastell R, Genant H, Grauer A, Cahall DL; IMPACT Study Group (2005) Underdiagnosis of vertebral fractures is a worldwide problem: the IMPACT study. *J Bone Miner Res* 20:557-563
- Hachiya Y (1994) MRI of compression and osteoporotic fracture (in Japanese). *MB Orthop* 7:173-185
- Nakano T, Abe Y, Shimizu Y, Ochi R, Seike I, Iwamoto K, Fujiwara K, Takagi K (1999) Rate of correct diagnosis for vertebral fracture by plain roentgenograms (in Japanese). *Fracture* 21:586-588

ORIGINAL ARTICLE

# Percutaneous vertebroplasty for elderly patients with unhealed osteoporotic spinal fractures

Atsushi Harada,<sup>1</sup> Yasumoto Matsui,<sup>1</sup> Hiroyasu Okuizumi,<sup>1</sup> Norimitsu Wakao,<sup>1</sup> Takeshi Suzuki<sup>2</sup> and Zenya Ito<sup>3</sup>

<sup>1</sup>Department of Orthopedic Surgery, National Center for Geriatrics and Gerontology, Hospital, Aichi,

<sup>2</sup>Department of Orthopedic Surgery, Shizuoka-Saiseikai Hospital, Shizuoka, and <sup>3</sup>Department of Orthopedic Surgery, School of Medicine, Nagoya University, Nagoya, Japan

**Background:** Vertebroplasty is a procedure in which bone cement is injected percutaneously into the vertebral body.

**Methods:** We used this technique with 15 patients who had pseudarthrosis or delayed union of osteoporotic spinal fractures with vacuum clefts, and in whom conservative treatment did not relieve persistent pain. The procedure was performed in a short time with little blood loss, and no generic complications, leakage of bone cement to blood vessels or the spinal canal, or neural compression.

**Results:** At 1 week after the operation, pain was eliminated in seven patients, alleviated in seven patients, unchanged in one patient, and worsened in none. The rate of alleviation or elimination of pain after 1 week and 6 months was 93% and 85%, respectively. Recurrence of the pain was seen in four cases, but this was caused by new spinal fractures in separate locations, confirmed with magnetic resonance imaging, in three patients, and by multiple myeloma in one patient.

**Conclusion:** Thus, vertebroplasty, which alleviates pain rapidly and with low invasiveness, is a new and promising therapy for osteoporotic spinal fractures in which conservative treatment has failed. It seems to provide a large benefit to elderly patients if performed with prudent care with regard to complications at the time of bone cement injection, and in conjunction with treatment for osteoporosis.

**Keywords:** osteoporosis, pain, spinal fracture, vacuum cleft, vertebroplasty.

## Introduction

Many elderly people with osteoporosis suffer from spinal fracture, and are troubled by pain and disability. Seventy-three percent of osteoporotic spinal fractures are morphometrical fractures, with the remainder

considered to be clinical fractures.<sup>1</sup> With morphometrical fractures there is no traumatic disruption of bone and symptoms tend to slight, such as decreased height. Treatment of the fracture itself is therefore unnecessary for most morphometrical fracture patients. With clinical fractures, however, symptoms tend to be severe, including strong back pain and high level of disability due to traumatic disruption of bone with intraosseous bleeding. Therefore, most patients require some type of conservative orthopedic treatment for more than 4 weeks. Afterwards, symptoms gradually improve, and patients can return to their normal daily lives by 12 weeks. Bone union is also obtained over the course of several months.<sup>2</sup>

Accepted for publication 27 January 2006.

Correspondence: Dr Atsushi Harada, MD, Department of Orthopedic Surgery, National Center for Geriatrics and Gerontology, Hospital, Gengo 36-3 Morioka, Obu, Aichi 474-8511, Japan. Email: aharada@ncgg.go.jp

However, if conservative treatment fails to result in adequate bone union, the spinal fracture progresses to pseudarthrosis with persistent pain.<sup>3,4</sup> This is one of the worst clinical courses for an osteoporotic spinal fracture. Until recently, the treatment for delayed union or pseudarthrosis of osteoporotic spinal fracture was either surgery, which is highly invasive, or no intervention if it was judged that the patient's health condition was too poor to withstand surgery. As a result, there are many elderly patients with osteoporotic spinal fractures who have had chronic pain and decreased activities of daily living (ADL) over a long term. Development of more appropriate therapy for such patients has been eagerly awaited.

Vertebroplasty is a procedure that was begun in France,<sup>5,6</sup> in which bone adhesion and fixing is obtained in a short time by percutaneous injection of bone cement (polymethylmethacrylate [PMMA]) into the fractured vertebral body through the pedicles under monitoring by X-ray fluoroscopy. This procedure may be of great benefit for these elderly patients.<sup>5,6</sup> It can be used even with frail elderly patients because of the low level of invasion. However, the outcome with this method has not yet been sufficiently investigated in Japan.

We performed vertebroplasty using PMMA for patients with pseudarthrosis or delayed union of osteoporotic spinal fractures, and in the present study examined the effectiveness and safety of this method.

## Methods

### Subjects

Selection criteria for vertebroplasty, regardless of sex or age, were that the patient have pseudarthrosis or delayed union of an osteoporotic spinal fracture with a vacuum cleft,<sup>3</sup> persistent pain that was resistive to conservative treatment, and reduced ADL.

### Vertebroplasty procedure

PMMA (Stryker, Limerick, Ireland) was used as the bone cement. Patients were given local or epidural anesthesia in an operating room. The first step after the anesthesia was a reduction maneuver by Bohler's method; high pads were placed under precordia and pelvic region of the patient in the prone position, and fracture reduction was achieved with the patient's own weight. Under close monitoring by X-ray fluoroscopy, 11-G or 13-G bone marrow biopsy needles (Accura Biopsy Systems, Gainesville, FL, USA) were inserted percutaneously to within the vacuum cleft of the vertebral body through the pedicles on both sides. After aspirating the fluid within the cleft, it was lavaged while confirming that the physiological saline injected from one side flowed easily to the

biopsy needle on the other side. Next, contrast medium was injected under fluoroscopic guidance, and it was confirmed that there was no leakage outside the vertebral body or into the blood vessels. If this could not be confirmed, the procedure was stopped at that point. If there was no leakage, bone cement polymerization was started and when it reached a certain hardness the bone cement was injected through the biopsy needle on one side until the vertebral body vacuum cleft was filled. If it was insufficiently filled, additional cement was injected from the opposite side. During this procedure, several doctors carefully and frequently checked for bone cement leakage outside the vertebra or into the blood vessels, and blood pressure fluctuations were regulated. After the bone cement had completely hardened, the patient was allowed to change body positions, and to walk starting on the same day.

### Background data

We assessed the physical condition and osteoporosis status of patients at baseline. Bone mineral density in the lumbar spine and femoral neck were measured using dual energy X-ray absorptiometry (DPX; Lunar, Madison, WI, USA). Roentgenograms of the thoracic and lumbar spine were also evaluated to identify prevalent spinal fractures.

### Outcomes

Major assessment items were the effect on pain, evaluated on four levels of eliminated, alleviated, no change, and worsened at 1 week, 6 months, and 12 months after the procedure, and the recurrence of pain. We evaluated invasiveness in terms of operation time, blood loss and amount of bone cement injected, as well as complications related to the injection of bone cement in addition to general postoperative complications.

### Ethical considerations

A protocol detailing the above procedure was approved by the ethics committee of our hospital, and written informed consent was obtained from all patients.

## Results

Between January 2001 and November 2004 there were 17 patients who met the selection criteria and consented to vertebroplasty. One patient withdrew his consent, so that the procedure was conducted with 16 patients. They included two males and 14 females with ages ranging 60–88 years and a mean age of 76.7 years. Mean bodyweight and height were 46.8 kg (range 32–58 kg) and 148 cm (range 133–165 cm), respectively. Mean bone mineral density in the lumbar spine and femoral

**Table 1** Patient characteristics before vertebroplasty

No.	Age	Sex	Body weight (kg)	Height (cm)	Lumbar spine BMD (g/cm <sup>2</sup> )	Femoral neck BMD (g/cm <sup>2</sup> )	Number of prevalent spinal fractures including surgical site	Treatment for osteoporosis
1	60	Male	58	165	0.612	0.589	1	Alendronate
2	66	Female	53	160	1.114	0.809	3	None
3	70	Female	48	140	0.837	0.64	1	None
4	74	Female	53	160	0.855	0.727	2	None
5	74	Female	44	146	1.056	0.767	3	None
6	75	Female	45	146	0.958	0.708	3	Vitamin D <sub>3</sub>
7	76	Female	53	147	0.875	Not examined	2	Vitamin D <sub>3</sub>
8	78	Female	54	145	Not examined	Not examined	3	None
9	79	Female	43	133	0.739	0.531	4	None
10	80	Female	53	158	1.014	Not examined	3	None
11	80	Female	32	135	0.862	0.563	1	None
12	82	Female	45	150	0.766	0.471	3	Vitamin D <sub>3</sub>
13	84	Female	37	147	0.649	0.373	3	Alendronate
14	85	Female	41	140	0.695	Not examined	3	Vitamin D <sub>3</sub> + etidronate
15	88	Male	43	148	Not examined	Not examined	3	None

BMD, bone mineral density; Vitamin D<sub>3</sub>, alfa-Calcidol.

**Table 2** Operative data

No.	Surgical site	Operation time (min)	Volume of bone cement injected (mL)	Blood loss (mL)	Anesthesia	Complications
1	T12	31	2	10	Epidural	None
2	T12	103	8	10	Epidural	None
3	T12	98	1.5	10	Local	None
4	L1	45	8	Negligible	Epidural	None
5	L1	60	6	Negligible	Epidural	None
6	T12	20	4	10	Epidural	None
7	L2	121	4	10	Epidural + Local	None
8	T12	24	8	10	Epidural	None
9	T11 & T12	36	Unclear	Negligible	General	None
10	L1	69	1.5	30	Epidural + Local	None
11	L2	22	Unclear	Negligible	Epidural	None
12	T12	67	5	Negligible	Epidural	None
13	T12	97	1	10	Local	None
14	L2	135	3.3	30	Local	None
15	T12 & L1	65	2.8□A 6	10	Epidural	None

L1, first lumbar vertebra; L2, second lumbar vertebra; T11, 11th thoracic vertebra; T12, 12th thoracic vertebra.

neck was 0.849 g/cm<sup>2</sup>, or 75.4% of young adult mean, and 0.618 g/cm<sup>2</sup>, or 68.3% of young adult mean, respectively. Six patients had already received alendronate, etidronate, or vitamin D<sub>3</sub> for their osteoporosis before the vertebroplasty, and continued the same medication thereafter (Table 1). The main complaint was long-term persistent pain in all patients, with only one who had complications with neural symptoms of the

legs. The mean number of prevalent spinal fractures including the surgical site was 2.5, ranging 1–4 (Table 1). Fourteen patients had a painful fracture in a single vertebra, and two patients in two vertebrae. The affected painful region was two 11th thoracic vertebrae, nine 12th thoracic vertebrae, four first lumbar vertebrae, and three second lumbar vertebrae; thus, the fractures were concentrated in the thoracolumbar spine (Table 2).