表 2. これまでに報告された膝 OA の候補遺伝子

膝 OA の候補遺伝子として報告されたもの	膝 OA および類縁疾患との関連
COMP (cartilage oligomeric matrix protein)	偽性軟骨無形成症
COL11A1 (human type-XI procollagen gene)	Stickler 症候群
COL2A1 (human type-II procollagen gene)	軟骨形成不全，脊椎骨端異形成症など多数
VDR (vitamin D receptor gene)	骨粗鬆症，骨棘形成
aggrecan	手指 OA
COL9A1 (human type-IX procollagen gene)	股関節 OA
COL9A3 (human type-IX procollagen gene)	股関節 OA
IGF1 (insulin-like growth factor 1)	手指 OA，脊椎 OA
CRTL1 (cartilage matrix protein gene 1)	手指 OA，股関節 OA
ER (estrogen receptor)	骨粗鬆症
PAPSS2 (3'-phosphoadenosine 5'-phosphosulfate synthase)	脊椎骨端異形成症
ASPN (asporin)	膝 OA
AnK	CPPD 沈着
CALM1 (calmodulin1)	股関節 OA
FRZB (serected frizzeled-related protein-3)	股関節 OA（女性）
IL-1	股関節 OA
MATN3 (matrilin 3)	手指 OA
IL-4L	股関節 OA
ADAM12 (metalloprotease)	股関節 OA

実験では骨吸収抑制薬により膝 OA にみられる骨棘形成が抑制されたという研究[36]もある．さらに Baltimore aging study[37]では，変形性関節症と骨粗鬆症の関連性は罹患関節によって異なると述べている．したがって現状では膝 OA と骨粗鬆症の関連性は示唆されるが，その作用機序は明らかではない．

11 性ホルモン

女性ホルモンであるエストロゲン（estrogen：ERT）は，骨に対しては骨吸収を抑制し形成を維持する作用がある．膝 OA に対しても ERT 補充療法が試行され，発症と進行に予防的に作用可能性を示した報告が散見されるが，統計学的な有意差は認められていない[38,39]．近年，ERT レセプターに対する遺伝子学的研究からも ERT は膝 OA に対する予防的効果が報告されており[40]，前項の骨粗鬆症との関連性においても今後の研究がまたれている．

12 微量栄養素

ビタミン A，C，E およびベータカロチンは，活性酸素による軟骨破壊の抑制と修復をうながす点で膝 OA の発症に対しては有効ではないが，進行の抑制や膝痛の軽減に効果があるという報告が多い[41,42]．近年，Wang ら[43]は 10 年間の縦断研究からビタミン C 摂取が軟骨変性に予防的に作用することを明らかにしている．また，ビタミン D は骨代謝の観点から膝 OA との関連性が研究されている．McAlindon ら[44,45]は Framingham study において血中 25-ハイドロキシビタミン D 濃度の低下は膝 OA の進行を助長すると報告したが，近年，Felson ら[46]は Framingham と Boston の二つのコホートに対する縦断調査からビタミン D と膝 OA の進行との間に有意な関連性は見出せなかったとしており，一定の見解が得られていない．

13 遺伝子

膝 OA は common disease のため遺伝形式は多因子遺伝であり，原因遺伝子よりも感受性遺伝子（susceptibility gene）として研究される場合が多い．膝 OA の遺伝性についての報告は，Kellgren ら[47]が手指遠位指節間（DIP）関節の OA である Heberden 結節と膝 OA の合併例を調べ，「generalized OA（GOA）」という疾患概念を提唱し遺伝的素因を示唆したのが最初である．その後，軟骨形成不全症や Stickler 症候群など膝 OA の一つのモデルとも考え

られる疾患の原因遺伝子としてCOMP（cartilage oligomeric matrix protein）やCOL2A1（human type-Ⅱ collagen gene）などが同定され，これを足がかりにして，変形性関節症に関する多くの遺伝子多型（genetic polymorphism）が発見された[48~50]（表2）．さらに，これらの遺伝子多型の相関解析が行われているが，膝OAに関しては近年asporinの報告があるものの，いまだ特定されてはいない．また，ビタミンD受容体遺伝子（vitamin D receptor gene：VDR）は骨粗鬆症と関連性があることから，膝OAへの影響についても注目され多くの研究が行われており[51~53]，VDR遺伝子は初期の膝OAに関連する（Chingford study）や膝関節の骨棘形成に影響する（Rotterdam study）など多くの報告がなされているが一定の結論にいたっていない．いずれにせよ，今後膝OAに対する感受性遺伝子の研究はさらに加速すると思われるが，本疾患の複雑な病態から考えると大規模な集団に対する遺伝子解析が望まれる．

おわりに

現在，わが国においてX線像上膝OAと診断される人は1,000万人を超えると推計される．膝関節は起立歩行といった人間のもっとも基本的な動作の要であり，その機能破綻はわれわれの日常生活動作（ADL）や生活の質（QOL）に大きな影響を与える．したがって，膝OAに対する予防や治療方法の確立に向けて今後も病態解明の努力が必要と考えられる．

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《シンポジウム》

骨関節疾患リハビリテーションの実学（運動器の10年）
―変形性膝関節症のリハビリテーション実学―

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内側型変形性膝関節症の発症危険因子

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内側型変形性膝関節症の発症危険因子*

新潟大学超域研究機構

大森 豪

はじめに

内側型変形性膝関節症（以下，内側型膝OA）は我が国における代表的な骨・関節の加齢性疾患であり，荷重関節である膝関節の機能が障害されるため中高年者のADL（activity of daily life）やQOL（quality of life）に大きな影響を与える．内側型膝OAの80％以上は1次性であり加齢に伴って発症するため，その病態や危険因子の解明には自然経過の把握が極めて重要である．我は，内側型膝OAの自然経過と危険因子を知る目的で長期の疫学調査（松代膝検診）を行ってきた．本稿では，この疫学研究を紹介し本研究から得られたX線上の内側型膝OAの発症危険因子について概説する．

対象と方法

松代膝検診の概要[1-3]

松代膝検診は，新潟県十日町市松代地区において毎年7月に行われる住民の総合検診に合わせて行った．初回検診は，1979年に40～65歳の男女1,844名を対象として行い，以後基本的に同一の集団を7年毎に縦断的に評価した．初回検診の受診者は1,327名で受診率は81％であり，以後3回の検診でも受診率は70％以上と比較的良好であった（表）．また，第1回検診の受診者のうち558名（女性494名，男性64名）が以後21年間に行われた3回の検診を全て受診していた．

検診内容は問診（事前アンケートを含む），視触診および膝X線撮影とし，基本的に4回の検診とも同一内容とした．問診では，全身的な項目として職業，日常活動性，全身合併症と既往歴，喫煙習慣などを調べた．膝関節については，外傷歴や加療歴，水腫の既往および歩行・階段昇降能について聞いた．視触診では全身的に歩容と下肢アライメント，腰椎，股関節可動域，円背やHeberden結節の有無について調べ，膝関節においては歩行時のthrustの有無と膝のアライメント，可動域，関節安定性，関節裂隙の圧痛や水腫の有無について評価した．膝関節のX線撮影は立位膝関節正面像を撮影し，内側型膝OAの病期をKellgren分類[4]に準じた5段階で評価しgrade-Ⅱ以上を膝OAと判定した（図1）．したがって，本論文における膝OAの表記はX線上の定義に基

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表1　松代膝検診における各検診毎の受診者数と受診率

	対象年齢(歳)	総受診者数(人)	女性	男性	受診率(%)
第1回検診（1979年）	40～65	1,327	1,075	252	81
第2回検診（1986年）	47～72	1,015	831	184	80
第3回検診（1993年）	54～79	1,562	907	655	87
第4回検診（2000年）	61～86	1,260	711	549	73

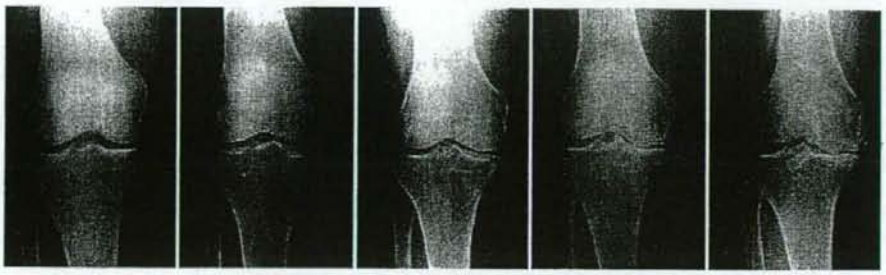

図1　Kellgren分類に準じた内側型変形性膝関節症のX線grade分類
Grade-Ⅱ以上を膝OAありと判定した.

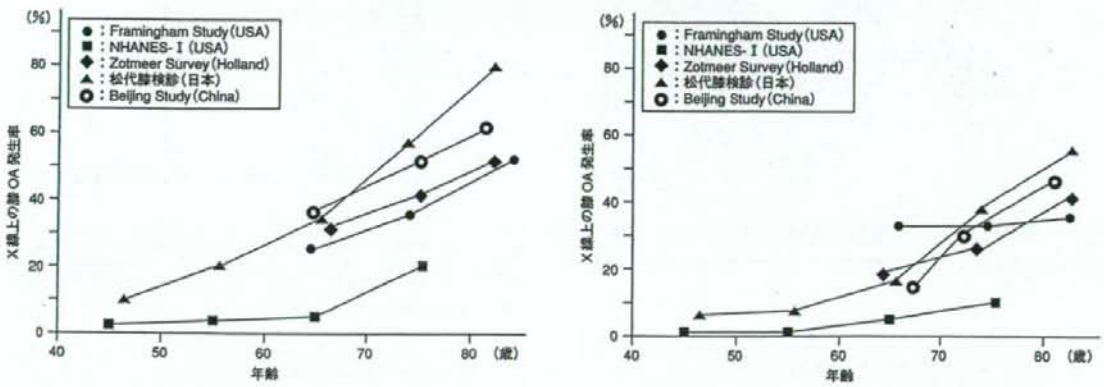

図2　松代膝検診および他の疫学調査による変形性膝関節症の発生率

づくものであり，疼痛，可動域制限や水腫といった本人の症状の有無は考慮されていない.

今回，2000年に行った第4回検診の横断的解析を行い，この結果から内側型膝OAの発症に関与する危険因子について検討した.

結　　果

1. 年齢，性別と内側型膝OAの発症

男女とも年齢の増加とともに膝OAの発生率も増加していた．女性では，40歳代で15%，50歳代で20%，60歳代で30%と増加し，70歳代では60%，80歳以上では80%以上が膝OAを生じていた（図2a）．男性でも，50歳代12%，60歳代20%，70歳代40%，80歳代60%と年齢に伴い膝OAが増加したが，その割合は女性より低くなっていた（図2b）．また，これまでに報告されている膝OAに関する代表的な疫学調査での発生率と比較すると，男女とも70歳以上の高齢域において発生率が若干高くなっていた.

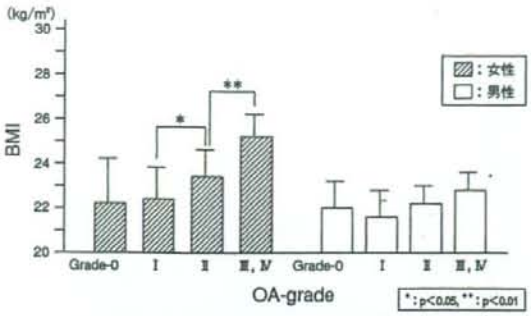

図3　肥満と内側型変形性膝関節症発生の関係
女性で膝 OA-grade の進行とともに BMI が有意に増加している．

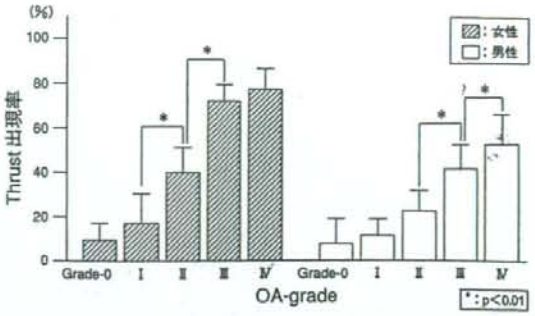

図5　Thrust 現象出現と内側型変形性膝関節症発生の関係
男女とも膝 OA-grade の進行とともに thrust 出現率が有意に増加している．

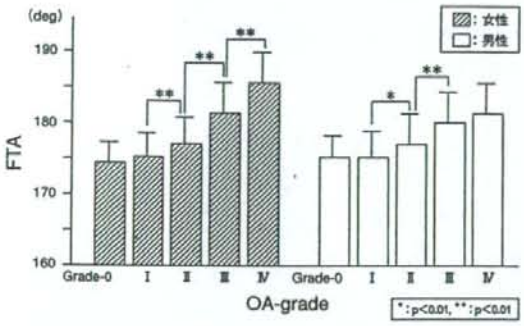

図4　膝内反変形と内側型変形性膝関節症発生の関係
男女とも膝 OA-grade の進行とともに FTA が有意に増加している．

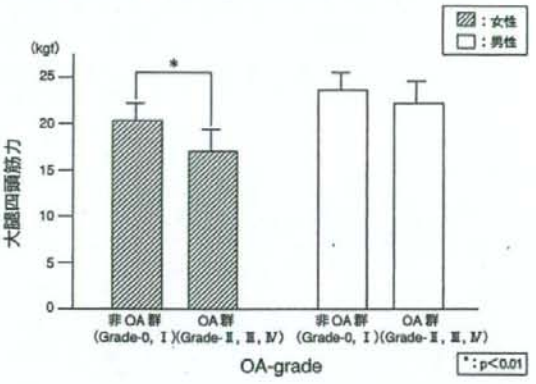

図6　大腿四頭筋力と内側型変形性膝関節症発生の関係
女性で OA 群（grade-Ⅱ，Ⅲ，Ⅳ）の大腿四頭筋力が有意に低下している．

2. 肥満と内側型膝 OA の発症

肥満の指標には BMI（body mass index）を用いた．女性では，膝 OA の grade が進行するにつれて有意に BMI が増加し，さらに grade-Ⅲ，Ⅳでは BMI の平均値が 25 kg/m² と BMI 上肥満と判定される割合も増加していた．これに対して男性では膝 OA の grade 進行に伴う BMI の増加は明らかではなく，全体的に肥満と判定される人も少なかった（図3）．

3. 内反膝変形と内側型膝 OA の発症

内反膝のアライメントを FTA（femollo tibial angle：大腿脛骨角）で評価した．男女とも膝 OA-grade の進行とともに FTA は有意に増加して膝内反変形の増強を認め，その傾向は特に女性で顕著であった（図4）．また，男女とも grade-Ⅰ からⅡの間でも FTA が有意に増加しており，内側型膝 OA において骨自体の変形が軽度な初期においても膝の内反が進行していることが明らかとなった．

4. Thrust の出現と内側型膝 OA の発症

歩行立脚初期に見られる膝の急激な内反運動（「横ぶれ」現象）である thrust の OA-grade 別の出現率を調べた．男女とも OA-grade の進行に伴い thrust の出現率が増加し，女性では grade-Ⅰ-Ⅱ間，Ⅱ-Ⅲ間で，男性では grade-Ⅱ-Ⅲ，Ⅲ-Ⅳ間で有意差を認めた．男女間の比較では，thrust 出現率は女性に多く認められた（図5）．

5. 大腿四頭筋力と内側型膝 OA の発症

簡易筋力測定器（アルケア社製 QH-302）を用いて膝伸展筋力を定量的に測定し，これを大腿四

頭筋力として膝 OA-grade との関係を評価した．Grade-0，Ⅰの非 OA 群と grade-Ⅱ，Ⅲ，Ⅳの OA 群の 2 群間で大腿四頭筋力を比較すると，男性では差が見られなかったのに対して女性では OA 群で有意に筋力が低下していた（図 6）．

考　察

疫学調査による膝 OA の発症悪化要因については，欧米を中心に現在まで多方面からの研究が行われている[5~12]．これまでに報告された因子の中で，肥満，女性，非喫煙，日常生活の活動性（職業歴，運動歴），膝関節外傷の既往，人種などは膝 OA との関与がある程度明らかになっているが，一方で骨粗鬆症，女性ホルモンなどは一定した見解が得られておらず，さらにビタミンやミネラル，抗酸化物質などの微量栄養素や遺伝子の関与については不明な点が多い．

我が国においても膝 OA に関する疫学調査の報告は散見されるが，いずれも対象集団が比較的小さくさらに横断調査が多いため，内側型膝 OA の発症悪化要因を明らかにするにはいたっていない[13~16]．近年，人種による差に注目して，我が国や中国において比較的大規模な母集団を設定して欧米の疫学調査と比較した研究も行われ，日本人女性では肥満，膝外傷の既往，職業の影響が大きいことや，中国では外側型の膝 OA の頻度が高いことなどが報告されている[17~19]．

我々が行ってきた松代膝検診は，対象集団の規模および縦断調査の期間から他に比類のない疫学調査である．今回，第 4 回の横断調査の解析から，加齢，女性，肥満，膝内反変形，thrust 現象，および大腿四頭筋力低下が内側型膝 OA と関連があることが明らかとなった．このうち，加齢，女性，肥満については他の報告と同様の結果であったが，膝内反変形，thrust 現象，大腿四頭筋力低下に関しての他の研究報告は少なく，松代膝検診から得られた貴重な研究結果の 1 つと考えられる[20,21]．我々は，内側型膝 OA の病態解明に対して疫学的手法と同時に生体力学的手法を用いて研究を行ってきた．その結果，下肢アライメントとしての膝内反変形および歩行時の thrust 現象は膝関節の内側荷重を増加させることを実験的にも明らかにしている[22,23]．これらの点から内側型膝 OA の発症・進行の機械的因子として膝内反変形および thrust 現象は極めて重要であり，さらに詳細な検討が必要と考えられる．今後，縦断調査の詳細な解析を行い各因子と膝 OA との因果関係を明らかにすることで危険因子を確定し，内側型膝 OA の発症・進行予防法の確立を目指すことが課題とされる．

松代膝検診の解析検討に際し，以下の諸氏の多大なる協力に深謝する．古賀良生（新潟こばり病院整形外科），渡辺博史，蕪木武史，菅原治美，浜田政晴（新潟こばり病院リハビリテーション部），田中正栄，西野勝敏（新潟県スポーツ医科学センター），遠藤和男，粟生田博子（新潟医療福祉大学），速水正，日向野行正（新潟大学医学部整形外科）．

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Original article

High tibial osteotomy using two threaded pins and figure-of-eight wiring fixation for medial knee osteoarthritis: 14 to 24 years follow-up results

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Abstract

Background. High tibial osteotomy (HTO) is an established surgical treatment for medial knee osteoarthritis (OA). Several studies have reported the deterioration of clinical results with time, especially after more than 10 years. The purpose of this study was to evaluate the long-term results after HTO using our originally developed fixation method and to clarify the factors affecting the long-term clinical outcome.

Methods. Sixty-eight HTO treatments in 55 patients were evaluated. Eighteen patients were unable to be analyzed, thus reducing the study to 48 knees in 37 patients. The follow-up rate of the knee joint was 70.6% and the mean follow-up period was 17.1 years. The first evaluation was performed at a mean of 6.5 years postoperatively, and the most recent evaluation was done at more than 10 years postoperative follow-up. A closing-wedge osteotomy was performed, and the osteotomy site was fixed with two threaded pins and a figure-of-eight wiring technique. The Japanese Orthopaedic Association knee rating score (JOA score) was used for the clinical assessment. The change of the femorotibial angle (FTA) and progression of knee OA were radiographically analyzed. The whole knees were subsequently divided into two groups, satisfactory group and unsatisfactory group, according to the JOA score at the most recent follow-up.

Results. The mean JOA score was 59.1 before HTO and 83.1 at the most recent evaluation. In comparing the satisfactory and unsatisfactory groups, the JOA score before HTO was the same, but the JOA score of the unsatisfactory group was significantly lower at the first evaluation. The FTA in the unsatisfactory group was the same as in the satisfactory group preoperatively, but it was significantly larger after HTO. The radiographic OA was significantly progressed at the most recent evaluation, but no difference was observed in the distribution of the preoperative OA grade between the two groups.

Conclusions. HTO with two threaded pins and figure-of-eight wiring fixation showed an acceptable clinical outcome, but careful attention was needed for correction loss in early postoperative periods. In addition, the proper correction angle is necessary in order to achieve satisfactory long-term results.

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Introduction

Osteoarthritis (OA) is the most common form of degeneration of the joints. The knee joint is the key structure in the lower extremity and has much influence on the activity of daily life (ADL) and the quality of life (QOL) in elderly persons. These include standing, walking, running, jumping, stair climbing, deep knee bending such as squatting or Japanese-style sitting, and other lower extremity tasks. Approximately 10% to 15% of people aged 60 years and older have symptomatic knee OA.[1] Therefore, knee OA is a major source of chronic disability and is becoming a serious public health problem.

High tibial osteotomy (HTO) is one of the successful surgical treatments for medial compartment knee OA. HTO was first described by Jackson and Waugh,[2] and it is now widely accepted as an attractive procedure with good pain relief and preservation of knee function. Previous studies of early to midterm results of HTO have shown excellent outcomes in more than 80% of cases.[3-5] However, several studies with long-term follow-up reported that the results of HTO deteriorated with time, especially after more than 10 years. Several factors have been identified as affecting the results of HTO, but they remain controversial. These include sex, age at surgery, body weight, preoperative severity of knee OA, method of osteotomy and fixation, correction angle, amount of preoperative adduction moment, and postoperative period.[6-14]

Among these factors, the type of fixation following osteotomy remains important, and, in the past, the following methods have been reported: bone staples, blade plate with screws, one third tubular plate with a cortical screw (tension bend principle), L-buttress plate, and external fixator.[3,15-20] We developed a fixation method using two threaded pins and figure-of-eight wire and used this method for our consecutive HTO cases.

The purpose of this retrospective study was to assess the long-term results after HTO using our fixation method and to clarify the factors affecting the long-term clinical outcome.

Subjects and methods

Our indications for HTO were basically as follows: (1) degenerative change was mainly located in medial compartment (medial knee osteoarthritis), (2) normal or mild degeneration in lateral and patello-femoral compartment, (3) patient was younger than 70 years old and had relatively high activity in ADL, and (4) good range of motion and no remarkable knee joint instability. Between 1980 and 1990, HTO was performed in 68 consecutive knees in 55 cases by our senior surgeon (Y. K.). Seven patients died, 6 patients were unable to be evaluated due to the presence of other severe medical illnesses, and 2 patients were lost to follow-up. Three knees in 3 patients were converted to total knee arthroplasty (TKA) at 10 years, 12 years, and 15 years after HTO, respectively. Therefore, the remaining 48 knees in 37 cases were available for the present study, and the follow-up rate of the knee joint was 70.6%. There were 43 knees in 33 women and 5 knees in 4 men. The mean age at HTO was 59 years with a range from 40 to 69 years. The mean follow-up period was 17.1 years, but individual follow-up ranged from 14 to 24 years. The preoperative diagnosis was medial compartment knee OA in all the cases, and the preoperative Kellgren-Lawrence classification[21] showed grade II in 8 knees, grade III in 35 knees, and grade IV in 5 knees. All of the patients were evaluated initially in 1993, with a mean follow-up of 6.5 years, and evaluated at more than 10 years follow-up postoperatively. All of the patients were fully informed about the procedures and gave their informed consent.

Operative procedures and postoperative regimen

In all knees, the closing-wedge interlocking osteotomy through a lateral approach was performed according to the technique described by Ogata.[22] The correction angle was preoperatively determined to allow the mechanical axis, which is the line connecting the center of the femoral head and the ankle joint, to pass through the midpoint of the lateral compartment. The preoperative planning was performed using non-weight-bearing supine radiograph of the whole lower extremity according to Ogata et al.[23] Ogata mentioned that the relative angle of the articular surface (condylar-plateau angle) in the weight-bearing knee changed after osteotomy, and this might give unpredictable results postoperatively. He also found that the condylar-plateau angle in the postoperative standing radiograph was very similar to that seen in the non-weight-bearing supine condition, and recommended that a non-weight-bearing supine radiograph was better for preoperative planning. The femorotibial angle (FTA) that met this condition was around 165° to 168° in the majority of cases. The fibula was resected at the mid portion of the shaft. The osteotomy site was fixed with two threaded pins and a figure-of-eight wiring technique. First, two threaded pins, 2.4 or 3.0 mm in diameter, were inserted from distal and lateral of the osteotomy site to the medial corner of the proximal tibia passing through the medial half of the osteotomy line. Next, figure-of-eight wiring, 0.8 to 1.0 mm in diameter, was placed between the distal end of the pins and lateral wall of the proximal tibia. After the osteotomy site was fixed, leg alignment was checked by X-ray and cancellous bone fragments harvested from the resected bone wedge were grafted to the osteotomy site (Fig. 1). Postoperatively, the knee joint was immobilized with a cast for 6 weeks. Range-of-motion exercise was started after the cast was removed. Partial weight bearing was started 4 weeks after HTO and full weight bearing was allowed at 8 to 10 weeks postoperatively.

Clinical evaluation

All of the patients were directly interviewed and examined. The clinical result was evaluated using the Japanese Orthopedic Association knee rating score (JOA score).[24] The JOA score consisted of four categories and 100 points as full marks: pain and walking (30 points), pain and ascending or descending stairs (25 points), range of motion (35 points), and joint effusion (10 points). In this study, the preoperative JOA score was compared with the JOA score at the first evaluation in 1993 and at the most recent follow-up. Subsequently, the results of the JOA score were classified as excellent if the most recent score was 91 to 100, good if 81 to 90, fair if 71 to 80, and poor if the most recent score was less than 70 points. Furthermore, all knee joints were divided into two subgroups according to the result of the most recent follow-up. The patients who were classified as excellent and good were referred to as the satisfactory group, and the patients who were classified as fair and poor were referred to as the unsatisfactory

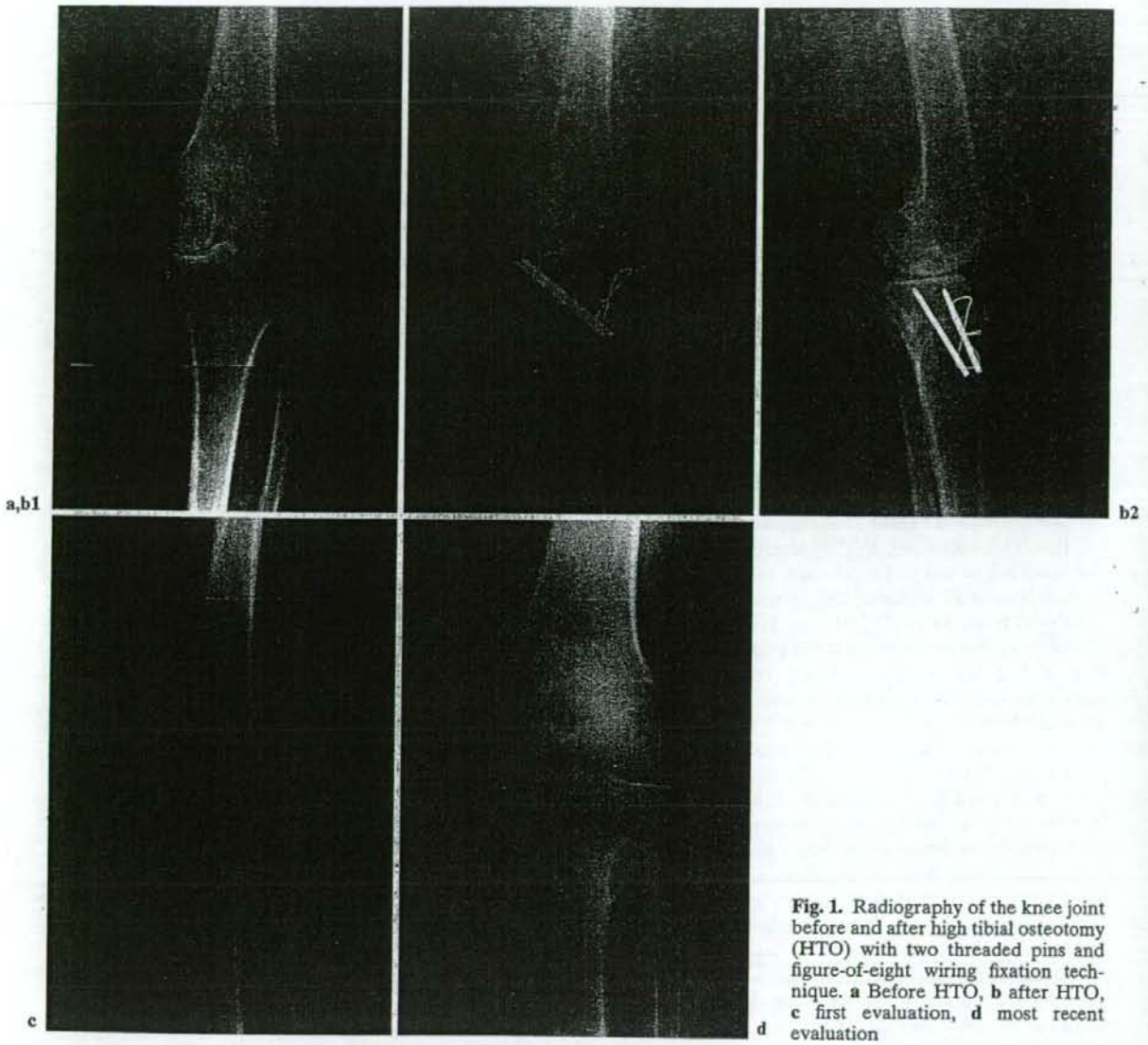

Fig. 1. Radiography of the knee joint before and after high tibial osteotomy (HTO) with two threaded pins and figure-of-eight wiring fixation technique. **a** Before HTO, **b** after HTO, **c** first evaluation, **d** most recent evaluation

group. Thirty-seven knees in 22 patients (1 male, 21 female) were included in the satisfactory group, with an average age at surgery of 57.9 ± 5.0 years and average follow-up period of 14.0 ± 2.9 years. On the other hand, 11 knees in 10 patients (3 male, 7 female) were included in the unsatisfactory group, with an average age at surgery of 60.1 ± 8.7 years and average follow-up period of 14.3 ± 3.1 years. No statistical difference was observed in the demographic data between the two groups.

Radiographic evaluation

The change of FTA and the grades of knee OA according to the Kellgren-Lawrence classification were analyzed with a standing whole-leg X-ray taken before surgery, at 1 to 3 weeks after HTO, and at each follow-up point.

Statistical analysis

The obtained data were expressed as the mean values ± standard deviation (SD). The relationships of analyzed parameters were determined using the paired *t*-test and the Wilcoxon signed rank test. In all analyses, a P value of less than 0.05 was considered to be significant.

Results

Clinical results

The mean JOA score of all patients improved significantly from 59.1 ± 7.6 before HTO to 86.3 ± 6.5 at the first evaluation (Table 1). At the most recent follow-up, the JOA score had slightly declined to 83.1 ± 9.3 but this change was not significant. In each category of JOA scores in all patients, the pain and walking score improved from 14.5 ± 5.2 before HTO to 26.6 ± 5.6 at the most recent evaluation, the pain and stairs score from 12.7 ± 6.6 to 20.2 ± 4.9, the score for range of motion from 25.6 ± 4.8 to 27.8 ± 4.6, and the score for joint effusion from 6.3 ± 5.7 to 8.5 ± 4.3. The mean range of motion was 9.3° ± 8.0° fixed flexion to 133.0° ± 18.1° of flexion before HTO, and 2.6° ± 4.3° to 132.5° ± 16.2° of flexion at the most recent evaluation. In comparing the satisfactory group and the unsatisfactory group, the mean JOA score was similar before HTO, but at the first and the most recent evaluation, the JOA score of the unsatisfactory group was significantly lower than that of the satisfactory group. Furthermore, in the unsatisfactory group, the JOA score had significantly declined from first evaluation to the most recent follow-up (Table 1). In the current study, there were two postoperative complications. One patient had peroneal nerve palsy and spontaneously recovered in 3 months after surgery. Another patient had delayed union and autologous iliac bone graft was performed. Final bone union was obtained at 7 months after HTO. These complications did not affect the clinical results.

Radiographic results

The mean FTA of all patients was corrected from 185.4° ± 4.4° before HTO to 168.2° ± 2.9° postoperatively, and this alignment was maintained at the most recent evaluation. In the satisfactory group, the change of FTA was almost same as the results of all patients. In contrast, the FTA of the unsatisfactory group changed from 185.3° ± 2.1° preoperatively to 170.2° ± 2.3° after HTO, and gradually increased at first evaluation and increased even more at the most recent follow-up. The FTA of the unsatisfactory group was the same as the satisfactory group preoperatively, but was significantly larger at each time of postoperative evaluation (Table 2). Seven of the unsatisfactory group (63.6%) had an FTA larger than 168° (170°: 3 cases, 172°: 3 cases, 173°: 1 case). The radiographic OA of all patients before HTO were classified as follows: 8 knees as Grade II, 35 knees as Grade III, and 5 knees as Grade IV. At the most recent evaluation, the distributions were 1 knee as Grade II, 18 knees as Grade III, and 29 knees as Grade IV. The number of Grade IV OA at the latest evaluation was significantly greater than that of before HTO (Table 3). In comparing the satisfactory group and the unsatisfactory group, no statistical difference was observed in the distribution of preoperative radiographic OA grade (Table 4). At the latest evaluation, the distributions of OA in the satisfactory group were 1 knee in Grade II, 18 knees in Grade III, and 18 knees in Grade IV. On the other hand, in unsatisfactory group, all knees were classified as Grade IV OA.

Table 1. Japanese Orthopaedic Association (JOA) score before high tibial osteotomy (HTO), at the first evaluation, and at the latest evaluation

Classification	Number of knees	JOA score		
		Before HTO	First evaluation[a]	Latest evaluation[b]
All Patients	48	59.1 ± 7.6	86.3 ± 6.5	83.1 ± 9.3
			**	
Satisfactory group	37	59.1 ± 9.1	90.0 ± 5.4	87.3 ± 4.3
			**	*
Unsatisfactory group	11	59.1 ± 5.8	82.2 ± 7.2	69.1 ± 5.8
			**	*

Data given as mean ± standard deviation
* $P < 0.05$; ** $P < 0.01$
[a] Mean follow-up 6.5 years
[b] Mean follow-up 17.1 years

Table 2. Femorotibial angle (FTA) before HTO, at the first evaluation, and at the latest evaluation

Classification	Number of knees	FTA (degrees)			
		Before HTO	After HTO	First evaluation[a]	Latest evaluation[b]
All Patients	48	185.4 ± 4.4	168.2 ± 2.9	169.1 ± 4.5	169.8 ± 5.2
Satisfactory group	37	185.5 ± 4.8	167.6 ± 2.8 *	168.0 ± 4.1 *	168.4 ± 4.4 **
Unsatisfactory group	11	185.3 ± 2.1	170.2 ± 2.3 *	172.7 ± 3.8 *	174.4 ± 5.2 **

Data given as mean ± standard deviation
* $P < 0.05$; ** $P < 0.01$
[a]Mean follow-up 6.5 years
[b]Mean follow-up 17.1 years

Table 3. Distribution of the radiographic osteoarthritis (OA) grade before HTO and at the latest evaluation

Classification	Number	OA grade[a]		
		Grade II	Grade III	Grade IV
Before HTO	48	8	35	5
Latest evaluation[b]	48	1	18	29**

** $P < 0.01$
[a]Radiographic OA grade according to the Kellgren-Lawrence classification
[b]Mean follow-up 17.1 years

Table 4. Distribution of the preoperative radiographic OA grade between the satisfactory group and the unsatisfactory group

Classification	Number	OA grade[a]		
		Grade II	Grade III	Grade IV
All Patients	48	8	35	5
Satisfactory group	37	8	26	3
Unsatisfactory group	11	0	9	2

[a]Radiographic OA grade according to the Kellgren-Lawrence classification

Discussion

The first purpose of this study was to evaluate our fixation methods. We used two threaded pins and figure-of-eight wire, and the basic concept of this procedure was similar to a tension band or modified tension band fixation as previously described.[17,18] Generally speaking, rigid fixation and early rehabilitation is important for good clinical outcome after HTO,[15,25] and there have been several studies concerning the primary stability of the implants for HTO.[26-28] Flamme et al.[27] tested the initial stability of the following devices: one third tubular plate with a cortical screw, blade plate with screws (Giebel's plate), bone staples, and external fixator. In their study, the highest stability was achieved by the bone staple and external fixator, while Giebel's plate and one third tubular plate were less stable. Recently, we biomechanically evaluated the initial stability of our fixation method and compared it with the bone staple, Giebel's plate, and L-buttress plate. The results of this study indicated that our method showed similar stability to Giebel's plate and the bone staple against compression and bending stress except rotational force.[29] In the present study, we additionally used cast immobilization after HTO in consideration of initial stability of our fixation method, and we clinically experienced 11 of 48 unsatisfactory cases. Furthermore, 7 of the unsatisfactory cases showed correction loss in early postoperative periods. The main reason for this early correction loss is thought to be combination of the lack of initial stability especially against rotational stress and the bone quality of the osteotomy site. Thus, we think the two threaded pins and figure-of-eight wiring fixation is an acceptable fixation procedure for HTO; however, careful attention should be paid to correction loss in the early postoperative periods.

The second purpose of the present study was to evaluate the long-term clinical results after HTO and to determine the factors related to the outcome. There are many studies about the clinical results after HTO. The

majority of authors have reported satisfactory results in the short to midterm, but these results gradually deteriorated over time, especially at more than 10 years after surgery. The reported probability of a good or excellent result after HTO was 75% to 96% after 6 years, 45% to 94% after 10 years, and 46% to 90% after more than 15 years.[3-14] In the current study, the percentage of satisfactory results (excellent or good) after HTO was 93.7% after 6 years and 77.1% after 17 years. Our results had the same tendency of deterioration over a long period as the other studies, but still maintained a favorable result up to 17 years after HTO. We think the main reason for the good clinical outcome in spite of the progression of radiographic OA is that good alignment was maintained in the majority of cases during the follow-up period and the ADL of the patients slowly deteriorated with time. Recently, Koshino et al.[14] evaluated 75 knees with a mean follow-up of 19 years and reported good or excellent results in 90% of their series. Good alignment was described as the most important factor for good long-term clinical results.[14]

There is still considerable discussion about which factors affect the long-term outcome of HTO, and the present study focused on the correction angle at the surgery and the preoperative severity of knee OA. As for the correction angle, previous studies have reported that the optimum clinical outcomes were associated with a correction of 6° to 16° valgus, and an undercorrection less than 5° was strongly related to a high failure rate.[5,8-14] In this study, the mean FTA after HTO was 167.6° in the satisfactory group and 170.2° in the unsatisfactory group. In addition, in the unsatisfactory group, progressive varus recurrence was found at the follow-up. We believe that the most important concept for HTO is to shift the loading axis from the medial compartment to the lateral compartment, and this will lead good long-term clinical outcomes in HTO. In order to achieve this safely, we recommend that we should target a valgus correction of at least 10° for medial compartment knee OA.

In western countries, the patients with advanced knee OA were primarily indicated for total knee arthroplasty. Therefore, there have been few studies that evaluate the relationship between the preoperative severity of the knee OA and the clinical result of HTO. Holden et al.[30] followed 51 knees for 10 years and found no correlation between the clinical results and the radiographic severity of the knee OA preoperatively. Rinonapoli et al.[10] evaluated 60 knees with an average follow-up of 15 years and their multivariate analysis indicated that the length of follow-up and the amount of preoperative osteoarthritis affected the clinical results. On the other hand, there have been many studies about this issue in Japan, because the preservation of range of motion is important for ADL in Japanese people. Yasuda et al.[8] found no statistical difference between the preoperative OA stage and the clinical results, but also described that no stage IV patients obtained good results. Sasazaki et al.[31] compared HTO in mild to moderate OA with advanced OA, and found no clinical difference between the two groups. They also indicated that overcorrection was effective for HTO in advanced OA cases.[31] In this study, the radiographic OA grade of the knee joint was significantly deteriorated at the mean follow-up of 17 years, but no statistical difference was observed regarding the preoperative severity of the radiographic knee OA between the satisfactory and the unsatisfactory group. Furthermore, three of five patients with preoperative Grade IV OA were included in the satisfactory group at the recent follow-up. Therefore, we agree that the mild to moderate stage is expected to have better results after HTO, but we could also expect good clinical outcomes for the advanced stage if the cartilaginous condition of the lateral compartment is acceptably preserved and the proper postoperative alignment is achieved.

We believe that there are two limitations in this study. The first limitation is that this is a retrospective study and the 70.6% follow-up rate is perhaps low even for the long-term periods of more than 10 years. The second limitation is that we used the JOA score for clinical evaluation. The JOA score is a good scoring system and is popular in Japan. In addition, several recent studies about HTO using this scoring system have been published in international journals.[24,32,33] However, even though the JOA score is not a worldwide universal measuring system, we believe that we can compare the result of this study with other clinical reports.

In conclusion, HTO with two threaded pins and figure-of-eight wiring fixation showed an acceptable and good clinical outcome for an average of 17 years of follow-up. The present study also suggests that the proper correction angle is necessary to achieve satisfactory long-term clinical results and HTO is considered to be indicated for the patients with a moderate to advanced stage of medial knee OA.

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透視X線像を用いた膝関節の3次元的位置姿勢の自動推定

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Accuracy of 3-D pose estimation of bone using an image matching technique with fluoroscopic images and 3-D bone model.

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Abstract

The mechanical perspective of bone and joint diseases can be gained through accurate measures of joint kinematics. This study attempted to develop an automated method for analyzing in vivo knee kinematics using single plane fluoroscopy and 3D bone models. The study was carried out on one human cadaveric knee. Three sphere markers were fixed to both femur and tibia. A 3D bone model was created by CT scan images of each bone.

After CT scanning, the femur and tibia were fixed using an external fixation device, resembling anatomical positions of the knee. Six single plane fluoroscopic images of 1 set of fixed bones were obtained with different directions of image acquisition. Digitally reconstructed radiographs (DRRs) were generated from 3D bone models by a voxel projection technique. The relative 3D-pose (full 6 degrees-of-freedom parameters) between femur and tibia were determined by matching the DRR of each bone model with the fluoroscopic image of the corresponding bone by automatic maximization of the similarity measure between the 2 images. The true value of the relative pose was measured using a 3D coordinate measuring machine. The RMSE of the in-plane rotation parameter was within 1.0 degrees and the out-of-plane rotation parameters were within 2.1 degrees. For the translation parameters the RMSE took its minimal value of 1.0 mm in the in-plane direction and its maximal value of 3.6 mm in the out-of-plane direction.

Key words : Knee, Kinematics, Single-plane fluoroscopy, Image matching.

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はじめに

関節の運動について定量的知見を得ることは，種々な関節疾患の病因解明や機能障害進行の把握において重要であると同時に，より効果的な診断・治療法の確立につながると考えられる．例えば，変形性膝関節症の治療法として多く施行されている人工膝関節置換術において，術前の人工関節の設置位置計画は静止状態で撮影した単純X線像やX線CT像を基に作成されるのみで，骨および関節の荷重状態での運動機能を考慮に入れて設置位置を決めることは行われていない．人工関節の寿命低下をもたらす摩耗や骨とのゆるみといった現象は，関節の運動に伴う動的負荷に起因するので，これを考慮に入れて設置位置を決めることが出来れば臨床的に有益である．

膝関節の運動を直接的な測定には，連続透視X線画像に対するイメージマッチングにより３次元位置姿勢を表す６自由度パラメータを推定する方法が提案され，人工膝関節置換術後の評価を目的とした動態解析に応用されている[1]．近年，この方法を人工関節が設置されていない膝関節に適用する試み[4]がなされているが，金属性の人工関節に比べ骨の輪郭は透視X線像上で明瞭では無いため，イメージマッチングの精度の点で改良の余地が残されている[3]．著者らは，X線CT撮影により予め構築しておいた３次元骨構造モデルを使って擬似X線像（Digitally Reconstructed Radiograph：以下DRR）を表示し，DRRに現れる輝度の濃淡を使ってイメージマッチングする手法[7]を提示したが，手動でイメージマッチングを行っていたため，作業に長時間を要するという問題点があった．そこで，本研究ではマッチングの高速化のため，滑降シンプレックス法による自動推定法を開発するとともに，同法の推定精度について検討することを目的とした．

実験方法

１．３次元測定器による真値測定

自動イメージマッチングによる３次元位置姿勢の推定精度を検証するため，３次元測定器により真値を測定した．ヒト切断膝１膝を用い，大腿骨および脛骨に直径15mmのアクリル製球マーカをそれぞれ３個ずつ任意の箇所に接着した後，創外固定器を用いて解剖学的位置関係を再現するように固定した．マーカの中心座標を３次元測定器（MITUTOYO：BH504 Coordinate Measuring Machine）で測定し，これから３次元測定器の座標系を基準とする各骨の座標系を決定した．この結果を基に脛骨を基準とする大腿骨の相対位置を求めた．

2．DRRの作製と表示

DRRに必要な3次元骨形状ボリュームモデルを作成するために，CT撮影を行った（機種：TOSHIBA社製 X-Vision，field of view：640×512［pixel］，pixel size：0.35×0.35［mm］，slice thickness：1［mm］）．閾値処理により骨領域を抽出して0.35×0.35×1.0［mm］のボクセルで構成されるボリュームモデルを作成した．さらに，DRR表示の高速化を図るため，スプライン補間により1辺が1mmの等方性（立方体）ボクセルに変換した．

DRRはボリュームモデルを構成する全てのボクセルを仮想X線照射点から画像平面に投影することで作成した（図1）．まず画像平面上において，一つのボクセルが投影された領域のX線量を$a\mu(x, y, z)$とした．ここで，aはX線の減衰を表す定数，$\mu(x, y, z)$はボクセル値である．そして，ある画素$p(u, v)$に着目すると，全てのボクセル（個数をNとする）の投影によってn個（$0 \leqq n \leqq N$）のボクセルが投影することになるので，次式によってその画素の輝度値を求めた．

$$I(u,v)=I_0 e^{-\sum_{i=1}^{n} a\mu_i(x,y,z)} \quad \cdots\cdots (1)$$

ここでI_0は輝度値の範囲である．aとI_0は実際の透視X線像とDRRのコントラストを合わせるため適宜調整する．

3．自動推定法

① 骨輪郭情報を用いた評価指標

透視X線像における骨の輪郭をCanny法[2]で自動抽出し，同時に抽出されたノイズを手動で除去した．次に，DRRの輪郭を表示し，輪郭点ごとに最も近い投影像の輪郭点との距離を求めてその平均値Iを計算し，類似度を表す評価指標とした（図2）．

$$I=\sum_{i=1}^{N} d_i \Big/ N \quad \cdots\cdots (2)$$

②輝度濃淡情報を用いた評価指標

透視X線像とDRRに対し，次式で表されるGradient difference[6]により両画像の輝度勾配

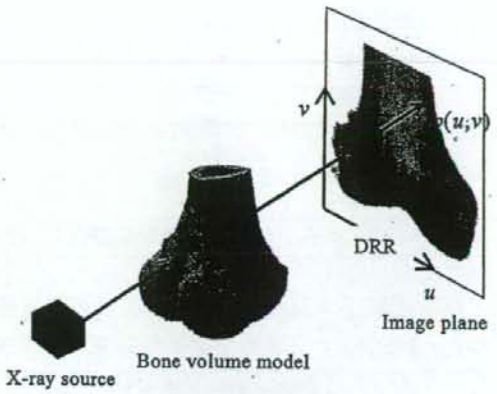

図1．Generation of DRR from bone volume model.

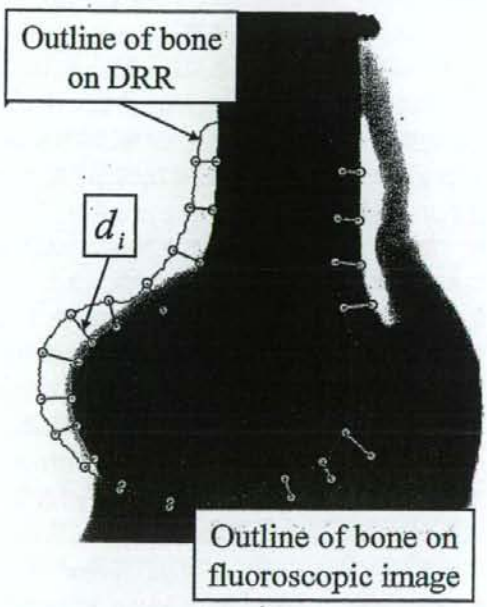

図2．Distance from a point of bone on DRR to the closest point of bone outline on fluoroscopic image.

分布の類似度を表す評価指標Gを求めた．

$$G(s)=\sum_{u,v}\frac{A_v}{A_v+(I_{diffV}(u,v))^2}+\sum_{u,v}\frac{A_h}{A_h+(I_{diffH}(u,v))^2}$$

$$\begin{cases} I_{diffV}(u,v)=\dfrac{dI_f}{du}-s\dfrac{dI_{DRR}}{dv} \\ I_{diffH}(u,v)=\dfrac{dI_f}{dv}-s\dfrac{dI_{DRR}}{dv} \end{cases} \quad \cdots (3)$$

ここで，I_fとI_{DRR}はそれぞれ透視X線像とDRRの輝度値，u，vは画像平面における水平