# Osteoarthritis and Cartilage



Association of radiographic and symptomatic knee osteoarthritis with health-related quality of life in a population-based cohort study in Japan: the ROAD study

S. Muraki †\*, T. Akune †, H. Oka ‡, Y. En-yo §, M. Yoshida §, A. Saika §, T. Suzuki ||, H. Yoshida ||, H. Ishibashi ||, F. Tokimura ||, S. Yamamoto ||, K. Nakamura ¶, H. Kawaguchi ¶, N. Yoshimura ‡

- † Department of Clinical Motor System Medicine, 22nd Century Medical and Research Center, Faculty of Medicine, The University of Tokyo, Tokyo, Japan
- ‡ Department of Joint Disease Research, 22nd Century Medical and Research Center, Faculty of Medicine, The University of Tokyo, Tokyo, Japan
- § Department of Orthopaedic Surgery, Wakayama Medical University, Wakayama, Japan
- Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
- ¶ Department of Sensory & Motor System Medicine, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

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#### SUMMARY

Objective: Knee osteoarthritis (OA) is a major public health issue causing chronic pain and disability. However, there is little information on the impact of this disease on quality of life (QOL) in Japanese men and women. The objective of the present study was to clarify the impact of radiographic and symptomatic knee OA on QOL in Japan.

Methods: This study examined the association of radiographic and symptomatic knee OA with QOL parameters such as the Medical Outcomes Study Short Form-8 (SF-8), EuroQOL (EQ-5D) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Radiographic knee OA was defined according to Kellgren/Lawrence (KL) grades, and symptomatic knee OA was defined as KL=3 or 4 with knee pain. We also examined the independent association of symptomatic knee OA and grip strength with QOL.

Results: From the 3040 participants in the Research on Osteoarthritis Against Disability (ROAD) study, the present study analyzed 2126 subjects older than 40 years who completed the questionnaires (767 men and 1359 women; mean age,  $68.9 \pm 10.9$  years). Subjects with KL = 3 or 4 had significantly lower physical QOL as measured by the physical component summary (PCS) score of the SF-8 and pain domains of the WOMAC, whereas mental QOL, as measured by the mental component summary (MCS) score of the SF-8, was higher in subjects with KL = 3 or 4 than KL = 0 or 1. Symptomatic knee OA was significantly more likely than radiographic knee OA without pain to be associated with physical QOL loss as measured by the PCS score and physical domains of the WOMAC. Symptomatic knee OA and grip strength were independently associated with physical QOL.

Conclusion: This cross-sectional study revealed that subjects with symptomatic knee OA had significantly lower physical QOL than subjects without it.

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# Introduction

Knee osteoarthritis (OA) is a major public health issue that causes chronic pain and disability<sup>1–3</sup>. The prevalence of radiographic knee OA is high in Japan<sup>4</sup>, with 25,300,000 subjects aged 40

years and older estimated to experience radiographic knee OA<sup>5</sup>. According to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan, OA is ranked fourth among diseases that cause disabilities that subsequently require support with activities of daily living<sup>6</sup>.

Quality of life (QOL) measurements in patients with chronic diseases are useful tools for estimating disease impact; these QOL scales may be generic or disease specific. Among the generic scales, the EuroQOL (EQ-5D) has been widely used to measure health-related QOL (HRQOL) in patients with OA<sup>7,8</sup>, and several studies have used the Medical Outcomes Study Short Form-36 (SF-36) in

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<sup>\*</sup> Address correspondence and reprint requests to: Shigeyuki Muraki, Department of Clinical Motor System Medicine, 22nd Century Medical and Research Center, Faculty of Medicine, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113-8655, Japan. Tel: 81-3-5800-9178; Fax: 81-3-5800-9179.

E-mail address: murakis-ort@h.u-tokyo.ac.jp (S. Muraki).

Caucasian patients with OA9-11. However, almost all of these studies include only patients with knee OA, and there are few population-based studies regarding knee OA and QOL<sup>11</sup>. A previous population-based study in Caucasians showed that arthritis has a major impact on the HRQOL measured by the SF-36 in a community setting<sup>11</sup>, although arthritis was examined by selfreported means and not by radiographs. In terms of disease-specific scales for knee OA, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has been used for Caucasians 12 and Asians 13,14, although these reports were not population-based studies. Furthermore, there is little information on the impact of knee OA with QOL in Japan, although a population survey suggests that the disease pattern differs among races 15-17. In fact, the prevalence of knee OA in Japan<sup>4</sup> was much higher than that of previous epidemiologic studies in elderly Caucasians<sup>16,18</sup>. Furthermore, in terms of risk factors, studies in Caucasians have suggested that occupational activities that include kneeling and squatting were associated with knee OA<sup>19</sup>, whereas these activities were not associated with Kellgren/Lawrence (KL) grades ≥ 2 OA in our previous study in Japan<sup>20</sup>. Therefore, the impact of knee OA on QOL also appears to differ in different populations. It would thus be of interest to clarify the impact of OA on QOL in a Japanese population.

The principal clinical symptom of knee OA is pain<sup>21</sup>, but the correlation with the radiographic severity of knee OA is controversial<sup>4,22–24</sup>. Thus it would be interesting to determine whether the impact of radiographic knee OA on QOL differs according to the severity of OA. Furthermore, pain is strongly associated with QOL, so it would be of interest to clarify the impact of symptomatic OA as well as radiographic knee OA on QOL.

Gender differences have also been observed in knee OA. The prevalence of knee OA is higher in women than men<sup>4</sup>, and the association of knee pain with knee OA also differs by gender<sup>4</sup>. Thus, the impact of these diseases on QOL may also differ between genders. However, to the best of our knowledge, there are no population-based studies that assess the association of knee OA with QOL in men and women separately.

Grip strength is a useful marker of muscle function and sarcopenia<sup>25</sup>. There is growing evidence that reduced grip strength is associated with adverse outcomes including morbidity<sup>26</sup>, disability<sup>27</sup>, falls<sup>27</sup>, higher fracture rates<sup>28</sup>, increased length of hospital stay<sup>29</sup>, and mortality<sup>27</sup>. A previous study also showed that grip strength is related to total muscle strength<sup>30</sup>. Furthermore, there is increasing recognition that grip strength is a useful clinical marker of sarcopenia, and recent work has validated this approach, demonstrating that grip strength is more strongly associated with age and is a better predictor of poor mobility than other potential markers such as calf muscle area<sup>31</sup>. Previous reports have shown that low muscle mass was also associated with reduced QOL<sup>32,33</sup>; thus, the association of knee OA with QOL may be influenced by grip strength, but again, no studies have examined the association of knee OA and grip strength with QOL simultaneously in the same population.

The first objective of this study is to clarify the association of radiographic severity of knee OA with QOL among Japanese men and women using the large-scale, population-based cohort study called the Research on Osteoarthritis Against Disability (ROAD). Because pain is strongly associated with QOL, we also examined the association of symptomatic knee OA with QOL. Finally, we analyzed the independent associations of knee OA and grip strength with QOL.

# Subjects and methods

## Subjects

The ROAD study is a nationwide prospective study designed to establish epidemiologic indexes for evaluation of clinical evidence

for the development of a disease-modifying treatment for bone and joint diseases (with OA and osteoporosis as the representative bone and joint diseases). It consists of population-based cohorts in several communities in Japan. A detailed profile of the ROAD study has been described in detail elsewhere 4,5,34; a brief summary is provided here. To date, we have completed creation of a baseline database including clinical and genetic information for 3040 inhabitants (1061 men and 1979 women) ranging in age from 23 to 95 years (mean, 70.6 years), who were recruited from resident registration listings in three communities: an urban region in Itabashi, Tokyo, a mountainous region in Hidakagawa, Wakayama, and a seacoast region in Taiji, Wakayama. All participants provided written informed consent, and the study was conducted with the approval of the ethics committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology. Anthropometric measurements included height and weight, and body mass index (BMI) (weight [kg]/height<sup>2</sup> [m<sup>2</sup>]) was calculated. Grip strength was measured on bilateral sides using a TOEI LIGHT handgrip dynamometer (TOEI LIGHT Co., Ltd, Saitama, Japan), and the better measurement was used to characterize maximum muscle strength. Among 2995 subjects aged 40 years or older in the ROAD study, 2243 (74.9%), 2245 (75.0%) and 2222 (74.2%) subjects completed the SF-8, the EQ-5D and the WOMAC, respectively, and 2126 (71.0%) subjects completed all three questionnaires. The present study analyzed 2126 subjects (767 men and 1359 women) aged 40 years (mean,  $68.9 \pm 10.9$  years) or older who had completed the SF-8, the EO-5D, and the WOMAC.

#### Radiographic assessment

All participants had radiographic examination of both knees using anterior-posterior and lateral views with weight-bearing and foot map positioning. Knee radiographs were read without knowledge of participant clinical status by a single well-experienced orthopaedist (SM) using the KL radiographic atlas for overall knee radiographic grades<sup>35</sup>. In KL grade, radiographs are scored as grade 0 through 4, with higher grades being associated with more severe OA. The higher KL grade in both knees was designated as that of the participant. Symptomatic knee OA was defined as: (1) a subject reporting knee pain lasting at least 1 month with pain having last occurred within the current or previous year; and (2) KL = 3 or 4 OA in the painful knee. To evaluate the intra-observer variability of KL grading, 100 randomly selected radiographs of the knee were scored by the same observer more than 1 month after the first reading. One hundred other radiographs were also scored by two experienced orthopaedic surgeons (SM & HO) using the same atlas for inter-observer variability. The evaluated intra- and inter-observer variabilities were confirmed by kappa analysis to be sufficient for assessment (0.86 and 0.80, respectively).

# Instruments

The SF-8 generates a health profile consisting of eight scales and two summary measures describing HRQOL. The SF-8 is an alternate form to the SF-36, which is the most widely used patient-based health status survey, translated into more than 40 languages; the Japanese version of the SF-36 has been well validated<sup>36</sup>. The SF-8 uses a single question to measure each of the eight SF-36 domains. In the SF-8, each of the eight items assesses a different dimension of health: General Health (GH), Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), Vitality (VT), Social Functioning (SF), Mental Health (MH) and Role Emotional (RE). The SF-8 was scored by assigning the mean SF-36 scale score from the 2002 general Japanese population to each response category of the SF-8 measuring the same concept, and then weighting each SF-8 item to

compute aggregate physical component summary (PCS) and mental component summary (MCS) scores. The SF-8 may be scored using a published algorithm for Japanese versions of the SF-8, which has been well validated<sup>37</sup>. The EQ-5D self-report questionnaire measures five domains of HRQOL, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression<sup>38</sup>. Each of the five domains is assessed by a single question with three response levels (no problem, some problems, and extreme problems), so the EQ-5D defines a total of 243 health states. These results were coded and converted to a score of utility using the tables of values<sup>39</sup>. The EQ-5D scoring algorithm was first developed using time trade off-based preference scores for a sample of these health states from a representative sample of the UK general population<sup>38</sup>; the Japanese version of the EQ-5D has been validated<sup>39</sup>. This EQ-5D algorithm is used worldwide and generates scores ranging from -0.111 to 1.000, with negative scores representing health states worse than being dead, 0 representing being dead, and 1.00 representing a state of full health. The WOMAC, a 24-item OA-specific index, consists of three domains: pain, stiffness, and physical function. Each of these 24 items is graded on either a five-point Likert scale or a 100-mm visual analogue scale 12,40. In the present study, we used the Likert scale (version LK 3.0). The domain score ranges from 0 to 20 for pain, 0 to 8 for stiffness, and 0 to 68 for physical function. Japanese versions of the WOMAC have also been validated<sup>41</sup>.

#### Statistical analysis

The differences in age, height, weight, BMI, grip strength, and QOL measurements between men and women were examined by the Student's t test. The prevalence of radiographic and symptomatic knee OA was compared between men and women using the chi-square test. We also used the chi-square test to analyze whether subjects with one symptomatic knee were likely to have symptomatic OA in the other knee. According to KL grade $^{35}$ , KL = 2 was defined as definite osteophytosis but no definite joint space narrowing, and KL=3 and 4 included definite joint space narrowing. We thus categorized KL grade in KL = 0 or 1, KL = 2, or KL=3 or 4, and differences among each KL grade with QOL measurements were determined using the Tukey Honestly Significant Difference (HSD) test without adjustment and after adjustment for age, BMI, and grip strength in men and women. We further classified subjects into those with symptomatic knee OA, those with KL = 3 or 4 knee OA without pain, and those without KL = 3 or 4 knee OA, and compared their association with QOL using the Tukey HSD test after adjustment for age, BMI, and grip strength. To determine the independent association of symptomatic knee OA and grip strength with QOL, we used multiple regression analysis without adjustment and after adjustment for age and BMI. Data analyses were performed using SAS version 9.0 (SAS Institute Inc., Cary, NC).

#### **Results**

The characteristics of the 2126 participants in the present study are shown in Table I. The prevalence of knee OA was significantly higher in women than men. The prevalence of bilateral and unilateral symptomatic knee OA was 2.0% and 3.0% in men, and 5.6% and 5.8% in women, respectively. Chi-square test showed that when the right knee had symptomatic knee OA, the odds ratio for the left knee to have symptomatic knee OA was 86.3 and 59.7 in men and women, respectively. The PCS and MCS of the SF-8 and the EQ-5D utility scores were significantly higher and the all domains of WOMAC were significantly lower in men than women, indicating that the QOL scores were higher in men than women.

**Table I**Characteristics of participants

	Overall	Men	Women	P-Values
Number of subjects	2126	767	1359	
Age, years	$68.9 \pm 10.9$	$69.7 \pm 10.5$	$68.4 \pm 11.1$	0.006
Height, cm	$154.6 \pm 9.2$	$162.8 \pm 6.7$	$150.0 \pm 6.9$	< 0.0001
Weight, kg	$55.0 \pm 10.9$	$61.5\pm10.8$	$51.4 \pm 9.0$	< 0.0001
BMI, kg/m <sup>2</sup>	$22.9 \pm 3.6$	$23.1 \pm 3.4$	$22.8 \pm 3.7$	0.03
Grip strength, kg	$25.5 \pm 9.3$	$33.2 \pm 8.9$	$21.2 \pm 6.3$	< 0.0001
Radiographic knee OA, %	17.9	11.6	21.5	< 0.0001
Symptomatic knee OA, %	9.0	5.0	11.3	< 0.0001
SF-8				
PCS	$47.0 \pm 7.0$	$47.4 \pm 6.8$	$46.8 \pm 7.0$	0.03
MCS	$52.8 \pm 5.9$	$53.4 \pm 5.3$	$52.5 \pm 6.1$	0.0009
EQ-5D	$0.90 \pm 0.15$	$0.91 \pm 0.14$	$0.90\pm0.15$	0.03
WOMAC				
Pain (0-20)	$1.37 \pm 2.44$	$1.13 \pm 2.16$	$1.50 \pm 2.57$	0.0003
Stiffness (0–8)	$0.71 \pm 1.25$	$0.63 \pm 1.09$	$0.77 \pm 1.33$	0.01
Function (0-68)	$4.08 \pm 7.93$	$3.35 \pm 7.06$	$4.49 \pm 8.37$	0.001

Except where otherwise indicated, values are the mean  $\pm$  SD.

The differences between men and women were examined by the Student's t test except for the prevalence of radiographic and symptomatic knee OA.

The prevalence of radiographic and symptomatic knee OA was compared between men and women using the chi-square test.

Radiographic knee OA was defined as KL grade 3 or 4.

Symptomatic knee OA was defined as KL grade 3 or 4 with knee pain.

SF-8, Medical Outcomes Study Short Form-8.

The scores for PCS and MCS in the SF-8, the EQ-5D utility scores, and all domains in the WOMAC by KL grade of knee OA in men and women are shown in Tables II and III. The associations of age, BMI, and grip strength with each QOL parameter were significant in men and women by linear regression analysis (P < 0.01), except for the association of age with the MCS of the SF-8. Thus, we used the Tukey HSD test after adjustment for age, BMI, and grip strength to determine the association of radiographic severity of knee OA with QOL. Men and women with KL = 3 or 4 had significantly lower QOL measured by PCS of the SF-8 and pain domains of the WOMAC than those with KL = 0 or 1 as well as KL = 2. In addition, the MCS scores were higher in men and women with KL = 3 or 4 compared with KL = 0 or 1. The EQ-5D utility scores were not significantly associated with the KL grade of the knee after adjustment for age, BMI and grip strength.

Next, to determine impact of symptoms of radiographic knee OA with QOL, we classified subjects into those with symptomatic knee OA, defined as KL=3 or 4 with knee pain, those with KL=3 or 4 without pain, and those without KL=3 or 4 and compared the impact of each type of OA on QOL using the Tukey HSD test after adjustment for age, BMI, and grip strength (Fig. 1). In men and women, PCS of the SF-8 and physical function domain of the WOMAC were significantly lower in subjects with symptomatic knee OA compared with those without KL = 3 or 4 knee OA (men: difference in mean -5.9, 95% CI -8.6 to -3.2 and difference in mean 4.9, 95% CI 2.2 to 7.6, respectively; women: difference in mean -4.3, 95% CI -5.7 to -2.9 and difference in mean 3.9, 95% CI 2.3 to 5.5, respectively) as well as KL = 3 or 4 knee OA without pain (men: difference in mean -6.3, 95% CI -9.7 to -3.0 and difference in mean 5.7, 95% CI 2.3 to 9.1, respectively; women: difference in mean -4.9, 95% CI -6.7 to -3.1 and difference in mean 3.9, 95% CI 1.8 to 5.9, respectively), whereas among those with KL = 3 or 4 knee OA without pain and no KL=3 or 4 knee OA, there were no significant differences in PCS of the SF-8 and physical function domain of the WOMAC. In women, MCS of the SF-8 was significantly higher in subjects with symptomatic knee OA compared with those without KL = 3 or 4 knee OA (difference in mean 2.6, 95% CI 1.3 to 4.0) as well as KL = 3 or 4 knee OA without pain (difference in mean 2.3, 95% CI 0.6 to 4.0). The EQ-5D utility score was

Table II
Mean scores of the SF-8, EQ-5D, and WOMAC scales by KL grade in men

		Severity of knee OA			Difference in means (95% CI)		
		KL = 0  or  1 (n = 444)	KL = 2 (n = 231)	KL = 3  or  4 (n = 92)	KL=3 or 4 vs KL=0 or 1	KL=3 or 4 vs KL=2	
SF-8							
PCS	Crude	$48.1 \pm 0.3$	$47.1 \pm 0.4$	$44.7 \pm 0.7$	-3.3 (-5.2, -1.5)	-2.3(-4.3, -0.4)	
	Adjusted	$47.8 \pm 0.3$	$47.4 \pm 0.4$	$45.5 \pm 0.7$	-2.3 (-4.2, -0.5)	-1.9 (-3.9, 0.0)	
MCS	Crude	52.8 ± 0.2	$53.7 \pm 0.3$	$55.3 \pm 0.5$	2.5 (1.1, 3.9)	1.6 (0.1, 3.1)	
	Adjusted	$52.9 \pm 0.3$	$53.7 \pm 0.4$	$55.2 \pm 0.6$	2.3 (0.8, 3.8)	1.5 (-0.02, 3.1)	
EQ-5D	Crude	$0.92 \pm 0.01$	$0.91 \pm 0.01$	$0.87 \pm 0.01$	-0.06 (-0.10, -0.02)	-0.04 (-0.08, 0.00)	
	Adjusted	$0.92 \pm 0.01$	$0.91 \pm 0.01$	$0.89 \pm 0.01$	-0.03 (-0.07, 0.01)	-0.03 (-0.07, 0.01)	
WOMAC							
Pain	Crude	$0.92 \pm 0.10$	$1.13 \pm 0.14$	$2.11 \pm 0.22$	1.19 (0.61, 1.76)	0.97 (0.36, 1.59)	
	Adjusted	$1.03 \pm 0.10$	$1.02 \pm 0.14$	$1.75 \pm 0.22$	0.72 (0.14, 1.30)	0.73 (0.12, 1.34)	
Stiffness	Crude	$0.57 \pm 0.05$	$0.65 \pm 0.07$	$0.91 \pm 0.11$	0.34 (0.05, 0.64)	0.26 (0.05, 0.58)	
	Adjusted	$0.60 \pm 0.05$	$0.61 \pm 0.07$	$\boldsymbol{0.80 \pm 0.12}$	0.20 (-0.10, 0.50)	0.19 (0.13, 0.51)	
Function	Crude	$2.83 \pm 0.33$	$3.38 \pm 0.46$	$6.08 \pm 0.73$	3.24 (1.36, 5.12)	2.70 (0.67, 4.73)	
	Adjusted	$3.31 \pm 0.32$	$2.88 \pm 0.45$	$4.66 \pm 0.72$	1.35 (-0.53, 3.23)	1.77 (-0.19, 3.74)	

Values are mean  $\pm$  standard error (SE). SF-8, Medical Outcomes Study Short Form-8.

Adjusted differences in means were calculated by Tukey HSD test after adjustment for age, BMI and grip strength.

significantly lower in subjects with symptomatic knee OA compared with those without KL=3 or 4 knee OA (difference in mean -0.08, 95% CI -0.13 to -0.02) as well as KL=3 or 4 knee OA without pain in men (difference in mean -0.08, 95% CI -0.15 to -0.01), but not in women.

Next, to examine the independent association of symptomatic knee OA and grip strength on QOL, multiple regression analysis was used with age, BMI, grip strength, and the presence of symptomatic knee OA as independent variables (Table IV). In men and women, symptomatic knee OA and grip strength were independently associated with PCS of the SF-8 ( $R^2$ , 0.11 and 0.17, respectively), EQ-5D utility scores ( $R^2$ , 0.08 and 0.12, respectively), and pain ( $R^2$ , 0.12 and 0.16, respectively), stiffness ( $R^2$ , 0.06 and 0.09, respectively) and physical function domains ( $R^2$ , 0.13 and 0.21, respectively) of the WOMAC.

#### Discussion

This is the first study to examine the association of radiographic and symptomatic knee OA with QOL measured by generic scales such as the SF-8, which is an alternate form of the SF-36, and the EQ-5D, as well as a disease-specific scale such as WOMAC in

Japanese men and women using a large-scale population-based cohort study. In the present study, subjects with KL=3 or 4 had significantly lower physical QOL than those with KL=0 or 1 as well as KL=2. At the same time, the MCS scores were higher in KL=3 or 4 than KL=0 or 1 in men and women. Furthermore, symptomatic knee OA was significantly associated with lower physical QOL compared with radiographic knee OA without pain. We further clarified the independent associations with symptomatic knee OA and grip strength. Symptomatic knee OA and grip strength were independently associated with lower QOL.

In the present study, physical QOL was significantly lower in subjects with KL=3 or 4 compared with KL=0 or 1 as well as KL=2 in men and women. Samsa *et al.* reviewed the existing literature and concluded that the Minimally Clinically Important Difference (MCID) for the SF-36 is typically in the range of 3–5 points<sup>42</sup>, implying that differences in SF-36 scores of 1–2 points are not important, but differences in scores of 3 points or more are clinically important. In this study, differences of PCS scores between subjects with KL=3 or 4 and those with KL=0 or 1 were 3.4 and 4.6 in men and women, respectively. The differences were similar to MCID thresholds, indicating that KL=3 or 4 knee OA may be clinically important for physical QOL. A previous study in China

Table III
Mean scores of the SF-8, EQ-5D, and WOMAC scales by KL grade in women

		Severity of knee OA			Difference in means (95% CI)		
		KL = 0  or  1 (N = 541)	KL = 2 (N = 526)	KL = 3 or 4 (N = 292)	KL=v3 or 4 vs KL=0 or 1	KL = 3 or 4 vs KL = 2	
SF-8							
PCS	Crude	$48.4 \pm 0.3$	$46.9 \pm 0.3$	$43.8 \pm 0.4$	<i>−</i> 4.5 ( <i>−</i> 5.7, <i>−</i> 3.4)	-3.0 (-4.2, -1.9)	
	Adjusted	$47.1 \pm 0.3$	$47.4 \pm 0.3$	$45.5 \pm 0.4$	-1.6 (-2.9, -0.3)	-1.9 (-3.1, -0.7)	
MCS	Crude	$52.1 \pm 0.3$	$52.3 \pm 0.3$	$53.8 \pm 0.4$	1.7 (0.7, 2.7)	1.4 (0.4, 1.5)	
	Adjusted	$51.9 \pm 0.3$	$52.5 \pm 0.3$	$53.8 \pm 0.4$	1.9 (0.7, 3.1)	1.3 (0.2, 2.4)	
EQ-5D	Crude	$0.92 \pm 0.01$	$0.89 \pm 0.01$	$0.85 \pm 0.01$	-0.07 (-0.09, -0.04)	-0.04(-0.07, -0.02)	
	Adjusted	$\boldsymbol{0.89 \pm 0.01}$	$0.91 \pm 0.01$	$0.89 \pm 0.01$	-0.003 (-0.04, 0.03)	-0.02 (-0.04, 0.01)	
WOMAC							
Pain	Crude	$0.96 \pm 0.11$	$1.45 \pm 0.10$	$2.62 \pm 0.15$	1.65 (1.23, 2.08)	1.16 (0.74, 1.59)	
	Adjusted	$1.45 \pm 0.11$	$1.19 \pm 0.11$	$1.99 \pm 0.15$	0.53 (0.07, 1.00)	0.80 (0.38, 1.21)	
Stiffness	Crude	$0.55 \pm 0.06$	$0.79 \pm 0.06$	$1.14 \pm 0.08$	0.59 (0.37, 0.81)	0.35 (0.12, 0.57)	
	Adjusted	$0.75 \pm 0.06$	$0.68 \pm 0.06$	$0.85 \pm 0.08$	0.10 (-0.15, 0.34)	0.16 (0.06, 0.39)	
Function	Crude	$2.41 \pm 0.34$	$4.54 \pm 0.35$	$8.32 \pm 0.47$	5.91 (4.54, 7.28)	3.78 (2.40, 5.16)	
	Adjusted	$4.37 \pm 0.35$	$3.62 \pm 0.33$	$5.79 \pm 0.47$	1.42 (-0.04, 2.88)	2.17 (0.85, 3.50)	

Values are mean  $\pm$  SE. SF-8, Medical Outcomes Study Short Form-8.

Adjusted differences in means were calculated by Tukey HSD test after adjustment for age, BMI and grip strength.

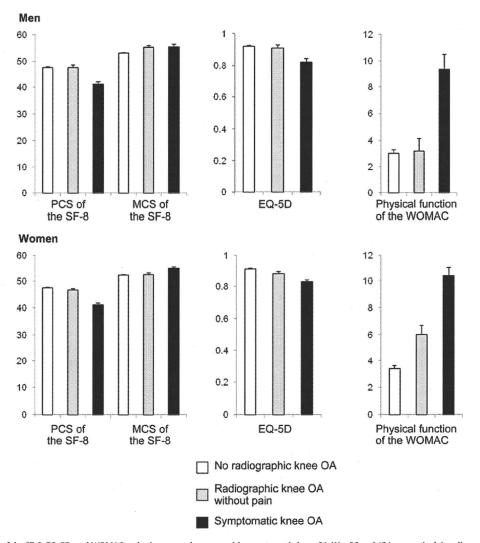


Fig. 1. Mean scores and SE of the SF-8, EQ-5D, and WOMAC scales in men and women with symptomatic knee OA (N = 38 and 154, respectively), radiographic knee OA without pain (N = 53 and 140, respectively), and no radiographic knee OA (N = 676 and 1065, respectively). Symptomatic knee OA was defined as KL = 3 or 4 with knee pain, radiographic knee OA without pain was defined as KL = 3 or 4 without knee pain, and no radiographic knee OA was defined as KL = 3 or 2.

also showed that subjects with severe knee OA had lower QOL than those with mild knee  ${\rm OA}^{14}$ , although their subjects were recruited from hospitals, so QOL parameters were not compared between subjects with mild knee OA and those without knee OA. The present study showed that there were no significant differences between subjects with KL = 2 and those with KL = 0 or 1. Considering the definitions of the KL grade, our findings may indicate that osteophytosis and joint space narrowing, which are representative features of knee OA, have a different impact on QOL. In other words, osteophytosis may have a weak impact on QOL, whereas joint space narrowing may have a strong impact.

Because QOL was shown to be strongly associated with pain, we next compared the impact of radiographic knee OA with and without pain on QOL. The present study showed that symptomatic knee OA was significantly associated with lower physical QOL than radiographic knee OA without pain. Differences in PCS scores among subjects with symptomatic knee OA and those without radiographic knee OA without pain were 6.6 and 6.5 in men and women, respectively. The differences were higher than the MCID; thus, symptomatic knee OA is considered clinically important for physical QOL. In addition, there were no significant differences in physical QOL between subjects with radiographic knee OA without

pain and those without radiographic knee OA. This finding indicates that loss of physical QOL was more strongly associated with symptoms such as pain due to radiographic knee OA rather than radiographic changes of the knee itself. In other words, QOL may improve when pain is relieved by medical care, even if subjects have radiographic knee OA.

As measured by MCS of the SF-8, knee OA was associated with higher OOL scores in men and women, although it was also associated with lower PCS. Past studies also showed the dissociation between PCS and MCS in knee OA<sup>43</sup>. Several factors may contribute to this phenomenon. First, the MCS questions within the SF-8 include generic questions about energy levels, feelings of being "downhearted and blue," and interference in daily activities as a result of emotional problems. These questions are less sensitive to the presence of mental health issues than disease-specific scales such as the Kessler psychological distress scale<sup>44</sup>. In fact, psychological distress has been shown to be significantly more frequent in those with arthritis than those without it, although scores on the MCS were not significantly different between these two groups<sup>45</sup>. Second, the dissociation may be due to a disability paradox<sup>46</sup>, which suggests that people with chronic disabilities report serious limitations in activities of daily living and problems in performing social roles, yet

**Table IV**Correlations of symptomatic knee OA and grip strength with scores of the SF-8, EQ-5D, and WOMAC scales

		SF-8		EQ-5D	WOMAC		
		PCS	MCS		Pain	Stiffness	Function
Men				100000000000000000000000000000000000000			
Symptomatic knee OA	Crude regression coefficient	-6.64 (-8.82, -4.46)	2.49 (0.77, 4.21)	-0.10 (-0.14, -0.05)	2.46 (1.78, 3.13)	0.83 (0.48, 1.18)	6.19 (3.95, 8.42)
(N=38)	Adjusted regression coefficient	-6.00 (-8.17, -3.81)	2.10 (0.33, 3.88)	-0.08 (-0.12, -0.03)	2.18 (1.51, 2.86)	0.75 (0.39, 1.10)	4.88 (2.67, 7.10)
Grip strength	Crude regression coefficient	0.20 (0.15, 0.25)	-0.03 (-0.07, 0.01)	0.003 (0.002, 0.004)	-0.06 (-0.07, -0.04)	-0.02 (-0.03, -0.01)	-0.23 (-0.28, -0.17)
	Adjusted regression coefficient	0.19 (0.12, 0.26)	-0.02 (-0.08, 0.03)	0.003 (0.001, 0.004)	-0.04 (-0.06, -0.02)	-0.01 (-0.02, 0.00)	-0.19 (-0.26, -0.12)
Women							
	Crude regression coefficient	-6.29 (-7.42, -5.16)	2.66 (1.64, 3.69)	-0.07 (-0.10, -0.05)	2.05 (1.64, 2.47)	0.80 (0.59, 1.02)	6.74 (5.40, 8.08)
(N = 154)	Adjusted regression coefficient	-4.36 (-5.52, -3.21)	2.52 (1.43, 3.61)	-0.03 (-0.06, -0.01)	1.44 (1.02, 1.85)	0.51 (0.29, 0.74)	3.97 (2.68, 5.27)
	Crude regression coefficient	0.34 (0.28, 0.41)	0.06 (0.01, 0.12)	0.007 (0.006, 0.009)	-0.11 (-0.13, -0.08)	-0.04 (-0.05, -0.03)	-0.46 (-0.53, -0.39)
	Adjusted regression coefficient	0.20 (0.13, 0.27)	0.08 (0.01, 0.15)	0.004 (0.003, 0.006)	-0.04 (-0.07, -0.02)	-0.01 (-0.03, 0.00)	-0.21 (-0.30, -0.13)

Adjusted regression coefficient is calculated by multiple regression analysis with age, BMI, grip strength, and the presence of symptomatic knee OA as independent variables. SF-8, Medical Outcomes Study Short Form-8.

state that they have excellent or good QOL. Many subjects with knee OA had knee pain, which may lead to functional impairment. Particularly in elderly individuals, pain or functional impairment may be considered a natural consequence of being elderly. Knee OA was thus not associated with lower scores for MCS in the SF-8.

In the present study, grip strength was independently associated with QOL measured by almost all domains of the three scales. Previous reports showed that low muscle mass was associated with reduced QOL<sup>32,33</sup>. There is increasing recognition that grip strength is a useful clinical marker of sarcopenia, and recent work has validated this approach, demonstrating that grip strength is more strongly associated with age and is a better predictor of poor mobility than other potential markers such as calf muscle area<sup>31</sup>. The independent association of grip strength with QOL suggests that QOL may improve with increase of muscle power in subjects with symptomatic knee OA, although longitudinal studies will be required to clarify this finding.

The present study showed that the association of radiographic and symptomatic knee OA with QOL differed among the SF-8, the WOMAC, and the EQ-5D. Radiographic and symptomatic knee OA were significantly associated with physical QOL in men and women, but not with EQ-5D utility scores. The reason for this difference may be explained by the fact that in the EQ-5D, all five domains are combined to analyze the association with knee OA, whereas the PCS and MCS of the SF-8 are analyzed separately. In fact, associations of knee OA differed between PCS and MCS of the SF-8, so when all domains were combined, the results may differ. For WOMAC, previous studies have found that WOMAC discriminates better among individuals with knee OA, whereas the SF-36 discriminates better among individuals with varying levels of selfreported general health status and comorbidities<sup>47</sup>. In addition, WOMAC was shown to be a more responsive measure than SF-36 in documenting changes after surgery $^{7,10}$ . Although our survey is not strictly comparable in design, it would appear that in our Japanese population, the PCS of the SF-8 and physical function domains of the WOMAC are able to discriminate among individuals with knee OA. It has been suggested that these two scales provide complementary information and may be useful in assessing both generic and disease-specific aspects of OA. However, this was a crosssectional study, so the efficacy of these scales for knee OA in a longitudinal analysis could not be clarified. In longitudinal studies, generic measures such as the SF-8 may be much less useful

than disease-specific measures such as the WOMAC because the generic measures pick up a lot of "noise" from comorbidities and may therefore be relatively unresponsive.

There are several limitations to the present study. First, this is a large-scale, population-based study, with a cross-sectional study of baseline data. Thus, causal relationships could not be determined. The ROAD study is a longitudinal survey, so further progress may help elucidate any causal relationships. Second, we did not include other weight-bearing OAs, such as hip OA, in the analysis, although this disorder may also affect OOL. However, the prevalence of KL = 3or 4 hip was 1.4% and 3.5% in Japanese men and women<sup>48</sup>, respectively, which was smaller compared with KL = 3 or 4 knee in the present study. Thus it is possible that hip OA would not strongly affect the results in the present study. Third, among the 2995 subjects ≥40 years old in the ROAD study, 2126 subjects had completed questionnaires for the SF-8, the EQ-5D, and the WOMAC, for a response rate of 71.0%. Subjects who completed questionnaires may have had better QOL than those who did not, so our results regarding QOL may have represented overestimations of QOL.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed that KL=3 or 4 OA was significantly associated with lower physical QOL scores, whereas KL=2 OA was not. Symptomatic knee OA was more strongly associated with QOL than radiographic knee OA without pain. Further studies, along with continued longitudinal surveys in the ROAD study, will help to elucidate the background of knee OA and relations with QOL.

#### **Author contributions**

All authors have made substantial contributions to all three of sections (1), (2) and (3) below;

- (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data
- (2) drafting the article or revising it critically for important intellectual content
- (3) final approval of the version to be submitted.

# **Conflicts of interest**

There are no conflicts of interest.

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#### References

- Sharma L, Kapoor D. Epidemiology of osteoarthritis. In: Moskowitz RW, Altman RD, Hochberg MC, Buckwalter JA, Goldberg VM, Eds. Osteoarthritis: Diagnosis and Medical/ Surgical Management. 4th edn. Philadelphia: Lippincott Williams & Wilkins; 2007:3–26.
- 2. Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, *et al.* The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health 1994;84:351–8.
- Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum 1998;41:1343-55.
- 4. Muraki S, Oka H, Akune T, Mabuchi A, En-yo Y, Yoshida M, et al. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. Osteoarthritis Cartilage 2009;17:1137—43.
- 5. Yoshimura N, Muraki S, Oka H, Mabuchi A, En-yo Y, Yoshida M, et al. Prevalence of knee osteoarthritis, lumbar spondylosis and osteoporosis in Japanese men and women: the Research on Osteoarthritis/osteoporosis Against Disability (ROAD). J Bone Miner Metab 2009;27:620–8.
- Ministry of Health, Labour and Welfare. The outline of the results of National Livelihood Survey 2007. Available at: http:// www.mhlw.go.jp/toukei/list/20-19-1.html.
- Brazier JE, Harper R, Munro J, Walters SJ, Snaith ML. Generic and condition-specific outcome measures for people with osteoarthritis of the knee. Rheumatology (Oxford) 1999;38: 870-7.
- Fransen M, Edmonds J. Reliability and validity of the EuroQol in patients with osteoarthritis of the knee. Rheumatology (Oxford) 1999;38:807–13.
- March LM, Cross MJ, Lapsley H, Brnabic AJ, Tribe KL, Bachmeier CJ, et al. Outcomes after hip or knee replacement surgery. Med J Aust 1999;171:235–8.
- Bachmeier CJ, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, et al. A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis Cartilage 2001;9:137–46.
- 11. Hill CL, Parsons J, Taylor A, Leach G. Health related quality of life in a population sample with arthritis. J Rheumatol 1999;26:2029–35.

- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833—40.
- 13. Thumboo J, Chew LH, Soh CH. Validation of the Western Ontario and McMaster University osteoarthritis index in Asians with osteoarthritis in Singapore. Osteoarthritis Cartilage 2001;9:440–6.
- Woo J, Lau E, Lee P, Kwok T, Lau WC, Chan C, et al. Impact of osteoarthritis on quality of life in a Hong Kong Chinese population. J Rheumatol 2004;31:2433—8.
- Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991—94. J Rheumatol 2006;33:2271—9.
- Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. J Rheumatol 2007;34:172–80.
- 17. Yoshida S, Aoyagi K, Felson DT, Aliabadi P, Shindo H, Takemoto T. Comparison of the prevalence of radiographic osteoarthritis of the knee and hand between Japan and the United States. J Rheumatol 2002;29:1454–8.
- 18. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham osteoarthritis study. Arthritis Rheum 1987;30:914–8.
- 19. Coggon D, Croft P, Kellingray S, Barrett D, McLaren M, Cooper C. Occupational physical activities and osteoarthritis of the knee. Arthritis Rheum 2000;43:1443—9.
- Muraki S, Akune T, Oka H, Mabuchi A, En-yo Y, Yoshida M, et al. Association of occupational activity with radiographic knee osteoarthritis and lumbar spondylosis in elderly patients of population-based cohorts: a large-scale population-based study. Arthritis Rheum 2009;61:779–86.
- Linaker CH, Walker-Bone K, Palmer K, Cooper C. Frequency and impact of regional musculoskeletal disorders. Baillieres Clin Rheumatol 1999;13:197–215.
- 22. Duncan R, Peat G, Thomas E, Hay E, McCall I. Croft P symptoms and radiographic osteoarthritis: not as discordant as they are made out to be? Ann Rheum Dis 2007;66:86–91.
- 23. Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27:1513—7.
- Neogi T, Felson D, Niu J, Nevitt M, Lewis CE, Aliabadi P, et al. Association between radiographic features of knee osteoarthritis and pain: results from two cohort studies. BMJ 2009;339:b2844.
- 25. Roubenoff R. Sarcopenia: a major modifiable cause of frailty in the elderly. J Nutr Health Aging 2000;4:4140–2.
- Sayer AA, Syddall HE, Dennison EM, Martin HJ, Phillips DI, Cooper C, et al. Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. QJM 2007;100:707–13.
- Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. J Geriatr Phys Ther 2008;31:3–10.
- Sirola J, Rikkonen T, Tuppurainen M, Jurvelin JS, Kroger H. Association of grip strength change with menopausal bone loss and related fractures: a population based follow-up study. Calcif Tissue Int 2006;78:218–26.
- Kerr A, Syddall HE, Cooper C, Turner GF, Briggs RS, Sayer AA.
   Does admission grip strength predict length of stay in hospitalised older patients? Age Ageing 2006;35:82

  –4.

- Wind AE, Takken T, Helders PJ, Engelbert RH. Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? Eur J Pediatr 2010;169:281

  –7.
- 31. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 2003;95:1851–60.
- Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J Gerontol A Biol Sci Med Sci 2002;57:M772

  –7.
- Sayer AA, Syddall HE, Martin HJ, Dennison EM, Roberts HC, Cooper C. Is grip strength associated with health-related quality of life? Findings from the Hertfordshire Cohort Study. Age Ageing 2006;35:409–15.
- 34. Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Cohort profile: research on osteoarthritis/osteoporosis against disability study. Int J Epidemiol (In press).
- 35. Kellgren JH, Lawrence JS, Eds. The Epidemiology of Chronic Rheumatism: Atlas of Standard Radiographs of Arthritis. Oxford: Blackwell Scientific; 1963.
- 36. Fukuhara S, Bito S, Hsiano A, Green J, Kurokawa K. Translation, adaptation, and validation of the SF-36 health survey for use in Japan. J Clin Epidemiol 1998;51:1045–53.
- 37. Fukuhara S, Suzukamo Y. Manual of the SF-8 Japanese Version (In Japanese). Kyoto: Institute for Health Outcomes & Process Evaluation Research; 2004.
- 38. Dolan P. Modeling valuations for EuroQol health states. Med Care 1997;35:1095–108.
- Japanese EuroQOL Translation Team. The development of the Japanese EuroQOL instrument. J Health Care Soc 1998;8:109—1123.
- 40. Barr S, Bellamy N, Buchanan WW, Chalmers A, Ford PM, Kean WF, *et al.* A comparative study of signal versus aggregate methods of outcome measurement based on the WOMAC osteoarthritis index. J Rheumatol 1994;21:2106–12.

- 41. Hashimoto H, Hanyu T, Sledge CB, Lingard EA. Validation of a Japanese patient-derived outcome scale for assessing total knee arthroplasty: comparison with Western Ontario and McMaster Universities osteoarthritis index (WOMAC). J Orthop Sci 2003;8:288–93.
- 42. Samsa G, Edelman D, Rothman ML, Williams GR, Lipscomb J, Matchar D. Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilities Index Mark II. Pharmacoeconomics 1999:15:141–55.
- 43. Boutron I, Rannou F, Jardinaud-Lopez M, Meric G, Revel M, Poiraudeau S. Disability and quality of life of patients with knee or hip osteoarthritis in the primary care setting and factors associated with general practitioners' indication for prosthetic replacement within 1 year. Osteoarthritis Cartilage 2008;16:1024–31.
- 44. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, *et al.* Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002;32:959–76.
- 45. Hill CL, Gill T, Taylor AW, Daly A, Grande ED, Adams RJ. Psychological factors and quality of life in arthritis: a population-based study. Clin Rheumatol 2007;26:1049–54.
- 46. Albrecht G, Devlieger P. The disability paradox: high quality of life against all odds. Soc Sci Med 1999;48:977—88.
- 47. Hawker G, Melfi C, Paul J, Green R, Bombardier C. Comparison of a generic (SF-36) and a disease specific (WOMAC) (Western Ontario and McMaster Universities Osteoarthritis Index) instrument in the measurement of outcomes after knee replacement surgery. J Rheumatol 1995;22:1193–6.
- 48. Inoue K, Wicart P, Kawasaki T, Huang J, Ushiyama T, Hukuda S, et al. Prevalence of hip osteoarthritis and acetabular dysplasia in french and japanese adults. Rheumatology (Oxford) 2000;39:745–8.

# V. 資料

[PRESS RELEASE]



2010年12月3日東京大学医学部附属病院

# 関節疾患総合研究講座 開発の膝関節診断支援ソフト KOACAD が Microsoft Innovation Award 最優秀賞を受賞

―変形性関節症の統合研究プロジェクト ROAD スタディの成果―

東京大学医学部附属病院 22世紀医療センター 関節疾患総合研究講座の岡敬之(助教)が株式会社イノテックと合同で開発した膝関節診断支援ソフト KOACADが、Microsoft Innovation Award 2010 最優秀賞を受賞しました。同センターで行っている変形性関節症の統合研究プロジェクト ROAD (Research on Osteoarthritis Against Disability) スタディ(※)の成果です。このソフトウェアは、健康に大きな影響を与えて社会問題にもなっている変形性膝関節症のレントゲン上での全自動診断に、世界に先駆けて成功したものです。医療ソフトでは初めての受賞で、12月2日の Microsoft Innovation Day (東京、九段)で発表されました。

【発表者】 岡 敬之(22世紀医療センター 関節疾患総合研究講座 助教)

吉村典子 (22 世紀医療センター 関節疾患総合研究講座 准教授)

中村耕三(22世紀医療センター長、整形外科・脊椎外科 教授)

川口 浩 (整形外科・脊椎外科 准教授)

# 【受賞の概要】

この度、東京大学医学部附属病院 22世紀医療センター 関節疾患総合研究講座の岡敬之(助教) が株式会社イノテックと合同で開発した膝関節診断支援ソフト KOACAD が、Microsoft Innovation Award 2010 最優秀賞を受賞しました。医療ソフトでは初めての受賞です。

Microsoft Innovation Award は、マイクロソフト株式会社が日本で今年1年に開発されたソフトウェアの中から、大きなイノベーションをもたらしたソフトウェアとその企業を表彰するものです。まず応募企業の中から、マイクロソフトの加治佐俊一最高技術責任者を委員長とする選考委員会により5つの優秀賞が決定されました。その後 Microsoft Tech·Ed Japan 2010 参加者約3,000 人、マイクロソフト全社員による投票、そしてマイクロソフト役員による最終選考により5つの中からひとつだけ最優秀賞が選ばれました。選考結果は12月2日のMicrosoft Innovation Day (東京、九段)で発表されました。

# 【受賞ソフトウェアの内容】

変形性関節症(osteoarthritis: 0A) は、高齢者の要支援・要介護原因疾患のそれぞれ第1位・第3位を占めており、高齢者の健康寿命の延伸、全国民の健康向上に大きく関与しています。中でも、変形性膝関節症は国内で患者数2400万人と推定されており、その予防法・治療法の開発は社会的にも焦眉の課題です。それにもかかわらず、変形性関節症の研究は国内・国外を通じて、他の生活習慣病に比べても明らかに遅れています。これは、糖尿病におけるへモグロビンA1cや骨粗鬆症における骨密度測定に相当するような定量評価法が、変形性関節症には存在していないためです。

当院 22 世紀医療センター(中村耕三センター長)では、2005 年より変形性関節症の統合研究プロジェクト ROAD (Research on Osteoarthritis Against Disability) スタディを樹立し、関節疾患総合研究講座の岡敬之が中心となって膝関節レントゲン画像の定量評価・客

観的重症度指標の確立に取り組んできました。その結果、ソフトウェア KOACAD (Knee osteoarthritis computer associated diagnosis) の開発に成功しました。このソフトウェアは、膝関節レントゲン画像において重症度指標(内・外側の関節裂隙の最小距離および面積、骨棘面積、大腿脛骨角)を瞬時に全自動で計測して定量値を出力するものです(添付資料参照)。従来のレントゲン読影においては評価者内および評価者間評価にばらつきが大きいことが問題となっていましたが、本ソフトの利用により一定で正確な重症度評価が可能になりました。

本ソフトウエアは岡敬之が独自に開発に着手し、株式会社イノテック (http://www.inotech.co.jp) と共同でバージョンアップをしたものです。

# 【今後の展望】

今回の受賞によって、KOACADが変形性膝関節症の評価基準の国際標準となることが十分に考えられます。国内外を通じて、変形性関節症の客観的な重症度指標の確立だけでなく、新たな治療法や予防法の効果判定に役立つものと考えています。

# 【参考文献】

- 1. Oka H, et al. Fully automatic quantification of knee osteoarthritis severity on plain radiographs. Osteoarthritis Cartilage 16: 1300-1306, 2008.
- 2. Oka H, et al. Normal and threshold values of radiographic parameters for knee osteoarthritis using a computer-assisted measuring system (KOACAD): the ROAD study. J Orthop Sci 15: 781-789, 2010.

# 【注意事項】

本件につきましては、報道解禁はございません。

## 【注釈】

※変形性関節症の統合研究プロジェクト ROAD (Research on Osteoarthritis Against Disability) スタディ:

変形性関節症の画期的な診断法・治療法の開発を目指した戦略的統合研究計画です。東大整形外科講座、22世紀医療センター の2つの講座 (関節疾患総合研究講座、臨床運動器医学講座)によって、臨床情報とゲノム情報を網羅した大規模統合臨床データベースの構築、分子生物学研究による軟 骨変性制御分子の解明、そして今回の受賞となった重症度評価システムの開発の3つのテーマについての研究を行っています。

#### 《本件に関するお問合せ先》

東京大学医学部附属病院 22 世紀医療センター 関節疾患総合研究講座

助教 岡 敬之

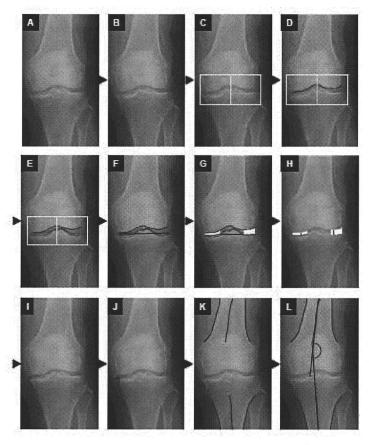
電話:03-5800-9178 (直通) E-mail:okah-tky@umin.ac.jp

#### 《取材に関するお問合せ先》

東京大学医学部附属病院 パブリック・リレーションセンター(担当:小岩井、渡部)

電話:03-5800-9188 (直通) E-mail:pr@adm.h.u-tokyo.ac.jp

# 【添付資料】



# KOACAD自動測定の工程

A→Lの手順で全自動測定し、重症度指標(内・外側の関節裂隙の最小距離および面積、骨棘面積、大腿脛骨角)を数値として瞬時に出力する。

Silverlight をインストールするには、ここをクリックします

Japan 変更 | サイトマップ

Microsoft

マイクロソフト サイトの検索

クエリ法

マイクロソフト イノベーション センター | 企業市民活動 (企業の社会的責任)

マイクロソフトについて マイクロソフト イノベーション センター ホーム ミッション

ファシリティ レポート セミナー / トレーニング

イノベーション デイ 地方協力団体

プログラム

MIC の多彩なプログラム IT ベンチャー支援プログラム ▶ Microsoft BizSpark

早期採用支援 お申し込みからサポートまで

IP ライセンス

IP (知的財産) ライセンスの ▶

標準規格ライセンス ライセンス取得方法 ライセンス ポリシー FAQ

IP カタログ

相互運用性 Interoperability 相互運用性

Open Up

お問い合わせ





English >>

#### Microsoft BizSpark 活用事例

#### 株式会社イノテック

Microsoft Innovation Award 2010 - BERTER

企業に必要な初期投資を大幅に抑制しながら、最新のソフトウェア開発環境を活用。 今後、多言語化展開を目指すうえで、ツールとマーケティング効果に期待。

Web サイトに「画像処理ソフトなら…」というキャッチコピーを掲げる株式会 社イノテックは、画像処理技術に定評がある、広島県の IT ベンチャー企業 です。ビデオ計測ソフト、座標計算ソフト、特殊計測ソフトなどを、国内工業 メーカー各社に OEM 製品として提供しています。

株式会社イノテックが所有する画像処理技術には、特許申請中の技術も含 まれているほか、研究機関が保持する特許の技術移転なども積極的に行 っています。東京大学医学部附属病院の岡 敬之 氏 (東京大学医学部付 属病院 22世紀医療センター 関節疾患総合研究講座 特任助教) との共 同研究により、変形性膝関節症診断支援ソフト「KOACAD」を開発。 Microsoft BizSpark を活用して、ソリューション開発を行い、Microsoft Innovation Award (MIA) 2010 では最優秀賞に輝きました。

# 株式会社イノテック inotech

「MIA 最優秀賞という名誉ある賞をいただき、大変喜ばしく思っておりま す。このような賞を受賞できたのも、岡先生やマイクロソフト関係者の皆様 との出会いがあり、社員全員の力を結集できたおかげです。これからも、開 発に携わっていただいた皆さん、そして、ご協力をいただいたマイクロソフト とともに、さらなる成長をしていきたいと思います」伊藤 賢治 氏 (株式会社 イノテック 代表取締役社長)

#### ソリューション概要

#### 株式会社イノテックロ

プロファイル 「お客様にリピートしていただけるソフトを目 指しています」という企業理念があらわすと おり、株式会社イケックは、お客様のニー ズをリザーチし、誰もが簡単に使いてなせ、 暑みでいただけるソフト開発を信念とする、 広島県の IT ベンチャー企業です。

広島県の IT ペンチャー企業でで) 画像処理技術に定評があり、ビデオ計測ソフト、座標計算ソフト、特殊計測ソフトなどの 製品を国内工業ペーカー各社に OEM として 提供、研究機関の特許に関する技術移転な ども獲怪的に行っており、同 敬之 氏(東京 大等医学部付属病院 2世紀医療センター 関節疾患総合研究講座 特任助教)との共 同研卒(アニリ(丁季私他振明物疾)を対す。 同研究により、「変形性膝関節症診断支援ソ フト KOACAD ロ Jを開発し、MIA 2010 最 優秀賞受賞。

## Microsoft BizSpark で利用したプログラ

- Visual Studio
- MSDN サブスクリプション

- 開発環境に必要となる初期費用をコスト
- 削減ソフトウェア購入申請に必要な時間を短
- 縮 多言語、多様なパージョン (過去から最 新版まで) の開発用ソフトウェアを活用 し、グローバル化や信頼性向上が図れ るなど、ソフトウェア品質の向上を実現

#### BizSpark 活用の背景とねらい

他社に真似することのできないテクノロジを活用してイノベーションを

株式会社イノテックは、画像処理技術に定評のある、広島県の IT ベンチャー企業です。これまでは、測定器/顕微鏡メー かー、パソコン/CCD カナラ関連メーカー、画像処理メーカーなどの工業メーカー各社を顧客とした。 で、工業向けのカスタム アブリケーションの開発や自社製品の OEM 提供を行っていました。当初は、Visual Basic を活 用していましたが、現在では .NET アプリケーションの開発も行っています。

「大きな転機となったのは、世界的な経済不況です。先行きが不透明になったため、工業メーカー各社の設備投資は減 少。IT 投資も例外ではなかったため、お客様からの受注は著しく減少しました。このような状況下で IT ベンチャーとして 身をたてるには、他社に真似することのできないテクノロジを活用し、画期的なソフトウェアを開発するほかに道はないと考 えていました」伊藤 賢治 氏 (株式会社イノテック 代表取締役社長)



伊藤 腎治 氏 (株式会社イノテック 代表取締役社長)

伊藤氏 (株式会社イノテック 代表取締役社長) が、目を向けたのは特許。各大学や研究機関により、開発された特許 (申請中を含む) を調査し、自社製品に応用できる技術を組み込むことで、他社にはまねできないソフトウェアの開発を行おうとしました。

はじめに行われた技術移転は、佐藤 和弘 氏 (広島工業大学 工学部 電気・デジタル システム工学科 教授) の「画像処理装置および画像処理方法」(特許: 3909604)。広島 TLO (技術移転機関) から紹介を受け、画像処理ソフト「QuickGrain」に移転しました。この技術移転は Web サイトなどでも取り上げられ、技術シーズを持つ各地の研究機関や TLO からさまざまな特許技術の紹介を受けるようにもなります。

「岡先生との出会いも、広島工業大学からの技術移転に関する記事をご覧いただいたのがきっかけです。東京 TLO からご紹介をいただき、X線画像による膝関節のすき間の面積や高さから、疾患の評価基準を数値化するという特許についてご説明をいただきました」伊藤 賢治 氏 (株式会社イノテック 代表取締役社長)

↑ページのトップへ

#### BizSpark 参加の経緯

両者の転機が、異業種参入と BizSpark 参加のきっかけに

株式会社イノテックにとって、医療ソリューションは新規参入。技術シーズを提案した、岡氏 (東京大学医学部付属病院 22世紀医療センター 関節疾患総合研究講座 特任助教) も、開発プロジェクトには異業種からの参入となります。

「4 年前までは診療だけを行っていましたが、変形性腰関節症に関するプロジェクトに参加したのをきっかけに、Visual Basic を勉強。他の言語も調査したのですが、情報量が足りず、一から勉強するにはあまり体系的でない印象を受けました。Visual Studio を活用することで、はじめての開発作業だったにも関わらず、アルゴリズムと具現化したプログラムを作成、学習さえすれば、誰もが使いこなすことのできる素晴らしい開発ツールです」岡 敬之 氏 (東京大学医学部付属病院22世紀医療センター 関節疾患総合研究講座 特任助教)



岡 敬之 氏 (東京大学医学部付属病院 22世紀医療センター 関節疾患総合研究講座 特任助教)

アルゴリズムがすでに具現化されたプログラムを見た、株式会社イノテックではすぐに技術移転を契約。共同研究を行うことになりました。

「医療ソリューションに参入したのも、岡先生との出会いがきっかけでしたが、Microsoft BizSpark 参加のきっかけもマイクロソフト社員の方との出会いがきっかけです。特許申請中(2006-279562)の画像処理技術ですでに契約していた岡先生の元を訪ねたところ、偶然にもその場にマイクロソフト社員の方が同席されました。その場で共同研究中のソリューションをご説明したところ、ご興味を抱いていただき、Microsoft BizSpark や Microsoft Innovation Award (MIA) についてご紹介を受けることができました」伊藤 賢治 氏 (株式会社イノテック 代表取締役社長)

↑ ページのトップへ

#### BizSpark 活用の効果

初期投資を大幅に抑制しながら、エンタープライズレベルの開発環境を活用

株式会社イノテックでは、出会いをきっかけに Microsoft BizSpark に登録。現在、2 名の開発者を登録し、統合開発ツールおよび開発用ソフトウェアをダウンロードして活用しています。社内でも、共同研究者である岡先生も、Visual Studioを活用していたため、すぐにその効果を実感しています。

「以前は開発ツールだけでなく、すべての開発環境を、その都度、購入し、開発と評価を行っておりました。Microsoft BizSpark では、条件を満たす IT ベンチャー企業に対して、統合開発ツール、開発用ソフトウェア、技術サポートなどが3 年間無償提供、ダウンロードするだけですぐに利用できます。通常、社内の購入申請には決裁を取るまでの時間が必要になりますが、Microsoft BizSpark のおかげで、コストも、申請の手間と時間も削減。迅速に開発作業が行え、機動力が向上しています」寺川 尚志 (株式会社イノテック 開発部 保長)



寺川 尚志 (株式会社イノテック 開発部 係長)

株式会社イノテックでは、Microsoft BizSpark の特典 (統合開発環境と開発用ソフトウェア) を存分に活用。岡氏 (東京 大学医学部付属病院 22世紀医療センター 関節疾患総合研究講座 特任助教) との共同研究により、膝関節診断支援ソ フト「KOACAD」を開発し、Microsoft Innovation Award 2010 最優秀賞を受賞しました。 Microsoft BizSpark の 特典は、MIA 受賞ソリューションだけでなく、日々の開発業務でも活用。利用できるツールやアプリケーションの豊富さにも 満足しています。

「Visual Studio Ultimate with MSDN と同等の特典が利用できるため、Visual Studio の最新パージョンを店頭でのリリースに先駆けて利用できたり、過去のオペレーディングシステムやアプリケーションを入手できたりするのも魅力的です。たとえば、以前に納品したソフトウェアの改修を依頼されることがありますが、Microsoft BizSpark に参加していなければ素果く対応できません。過去から最新まで、様々なブラットフォームでの動作確認をすぐに行うことができるため、大手のソフトウェア開発企業と同等の開発環境を手にできたと言えます。このように、Microsoft BizSpark では、開発作業のランニングコストや準備時間を削減できるだけでなく、製品品質の向上にも大きく役立つのです」寺川 尚志 (株式会社 イノテック 開発部 係条)

↑ページのトップへ

#### 今後の展望

多くの言語やシステム環境に対応し、より信頼性の高いソフトウェア提供を目指して

レントゲンは開発されてからこれまでの間、医師による誘影が基本であり、定量化する試みは行われてきませんでした。 関節診断支援ソフト『KOACAD』は、画期的なソリューションとして国内外の医療機関から評価を得ています。

「たとえば、骨粗しょう症は骨密度の測定が行われたことで、飛躍的に研究が進み、薬の開発にもつながりました。このように測定ツールは非常に重要で、数値化することで一定の結果を得ることができ、医療の進歩と標準化につながります。変形性関節症の治療は、厚生労働省の評価もいただいているほか、世界的にも注目。米国立衛生研究所(National Institutes of Health、NIH)や英国のケンブリッジ大学からも問い合わせをいただいています」図 敬之 氏(東京大学医学附属病院 22 世紀医療センター 関節疾患総合研究講座 助教)

今後、藤関節診断支援ソフト『KOACAD』の機能追加と信頼性の向上を図り、総合病院様や皆様がかかりつけのお医者 様でも簡単にご利用いただけるようなソフトウェアにしていくのが、株式会社イノテックの目標です。また、海外からの問い 合わせにも対応するため、グローバル展開も予定しており、各国語 OS の多様なパージョン上での動作チェックにも、 Microsoft BizSpark を活用していく予定です。

「Microsoft BizSpark の活用は、無償でダウンロードした開発環境だけでも、数百万のコスト削減効果があります。また、Microsoft Innovation Award 優秀賞受賞企業に選抜されたことで、マイクロソフトに選ばれたソフトウェア開発企業に仲間入りすることもできました。今回の受賞によるメディア露出によるマーケティング効果も期待できます。IT ベンチャー企業の皆様には、こんなにもさまざまな効果のある、Microsoft BizSpark をぜひ効果的に活用してくださいとお伝えしたいです」伊藤 賢治 氏 (株式会社イノテック 代表取締役社長)

Microsoft Partner Network (MPN) について説明を受けた伊藤氏は、現在、認定パートナーとなるべく、コンピテンシーの取得を検討中です。ISV 様の場合は、資格取得だけでなく、自社のアプリケーションを登録し、検証ツールで得た検証結果で参加要件を満たすことも可能。今回の受賞ソリューションや画像処理ソフトの一般ユーザー向けアプリケーションに対して、検証ツールを使用できます。伊藤氏は、将来、認定パートナー企業になることで、Microsoft BizSpark と同等の特典を活用できるだけでなく、Microsoft Pinpoint によるソリューション紹介やパートナー企業同士の交流をビジネスマッチングにつなげたいなど、さまざまな利用効果にも期待しています。



↑ ベージのトップへ

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#### プロファイル (個人情報) の管理

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いると診断した事例=東京大提供 画像解析ソフトで、ひざが変形して

# じかばめられます ひざ痛等がある場合 近くの病院にて受診 てください





者を少なくできると期待されている。 は欠かせず、病気が進行して寝たきりになる高齢 バラバラだった。早く見つけて予防するには基準 2500万人の患者がいるとみられ、厚生労働省 る「変形性関節症」。予備軍を含めひざだけで 研究班(主任研究者=中村耕三東京大教授)が統 した診断基準づくりを始めた。これまで診断は ひざなど関節の変形で慢性的な痛みに悩まされ (杉本宗)

#### 期 **# 2500** 者 推 発 万人

ないことが一因。骨粗鬆症は 伝が広く知られるようになっ 診断基準を作って病気や予防 こ、分かりやすい診断基準が 東大の川口浩准教授による

ものだとの報告もある。 症と分かることも多いとい 間に病気が進行して、悪化し 研究班が2005~07年に和 の約10%が関節の障害による つ。日本で寝たきりの高齢者 線を撮って初めて変形性関節 ケガなど別の治療でエックス やすい。東大病院でもひざの 割にとどまっており、知らぬ を調べて割り出した。 歌山県や東京都内の約3 自覚症状があるのは2~4 2500万人という推計は として診断基準を作り、予防 トゲがあるか、関節のすき間 が狭くなっているかなど見た で判定できる画像解析ソフト 班メンバーの岡敬之東大助教 に役立てることにした。 目で判断しているので、 医師ごとに、関節部分に骨の を開発した。ソフトでは、関 形性関節症の危険度を3段階 が、エックス線の写真から変 つきが大きいという。 変形性関節症でも、

研究班

で、すでに研究班メンバーが 社が発売した。 医療機関向け

研究

医大など8施設で導入。 いる慶応大や新潟大、

して学会などで基準値を議論

準値を設定するがソフトを使

データなどを参考に医者が基

って症例を積み重ねる。並行

ばら

ソフトは広島県のソフト会

を判定の材料とした。

の大きさ、O脚かどうかなど

番薄い部分の状態、 節のすき間の面積、

軟骨の 骨のトゲ

しかし、変形性関節症は

関節の軟骨がすり減ったり、 関節の周 囲に骨のトゲが生じたりして、 痛みや変 形を引き起こす病気。股関節や手足・背骨 の関節でも起こる。加齢や肥満、力仕事な どで関節に負担がかかることが原因とみ られる。軽症なら、筋肉を鍛える運動療法 や消炎剤などで痛みを和らげることがで きる。症状が進むと人工関節手術が必要 になることもあり、2008年度に手術を受 けたのはひざと股関節で推定約10万人。

変形性関節症

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