Policy of the Japanese Urological Association on PSA-based Screening for Prostate Cancer

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Background
The exposure rate for prostate cancer screening using prostate-specific antigen (PSA) is still very low compared with that in the USA or Western Europe. Consequently, in Japan about 30% of newly detected prostate cancer cases have bone metastases and many clinically significant cancer cases may go undetected or be missed until the disease is clinically advanced. Moreover, incidence rates for prostate cancer have continued to increase and are expected to increase in the future, with the number of newly diagnosed prostate cancer cases expected to reach 78,468 in 2020, making prostate cancer the second most prevalent cancer amongst men after lung cancer. The mortality rate for prostate cancer will also increase in the future and by 2020 is expected to be 2.8 times higher than that in 2000. Urgent implementation of the best available measures for effectively decreasing deaths from prostate cancer is therefore imperative. The Cancer Countermeasure Fundamental Law, an important national policy published in Japan in 2007, aims for a 20% decrease in the mortality rates for cancer in Japan within 10 years. The Japanese Urological Association has a policy of facilitating and promoting PSA-based screening for prostate cancer based on a well-balanced fact sheet including updated reviews on screening, diagnostic procedures and treatment for prostate cancer in human dry dock, as well as population-based screening for prostate cancer, following the successful decrease of mortality achieved in the USA since 1992.

Literature Review
The exposure rate for PSA screening in the USA is very high at approx. 75% in the 50 years and above age group. According to research on trends in prostate cancer mortality rates based on the cancer registry in the USA, the mortality rates for prostate cancer have continued to decrease since 1992, showing a 34% decrease between 1990 and 2004.1 Because there is no effective first prophylaxis to prevent the development of prostate cancer, that drastic decrease in the mortality rate for prostate cancer may be due to PSA screening and appropriate treatment strategies. According to the most recent ecological study carried out in the USA, there is a positive relationship between the incidence rate for distant metastases and the mortality rate of prostate cancer; and a negative relationship between PSA utilization and the incidence of distant metastases.2 In the other words, PSA screening can decrease the incidence of distant diseases, which may lead to a decrease in deaths from prostate cancer. Two large prospective randomized controlled trials investigating the impact of PSA screening on mortality for prostate cancer are now ongoing in the USA and Europe. The most recent publications from the European Randomized Study of Screening for Prostate Cancer (ERSPC) demonstrate that the incidence of advanced prostate cancer cases, defined as metastatic prostate cancer and cancer with pretreatment PSA levels above 100 ng/ml, significantly decreased (49%) in the screening arm compared with the control arm.3 The prognosis for advanced prostate cancer is worse than
that for cancer detected at an earlier stage. Therefore, the results of this research, conducted by ERSPC Sweden, must be recognized as a high priority study in the field of prostate cancer screening. According to the latest Tyrol study results, the exposure rate for screening was extremely high at 86.6% in 2005, and the incidence rate for metastatic prostate cancer has decreased by 70%. Moreover, the mortality rate for prostate cancer has decreased dramatically to 54% compared with the expected mortality rate. Because all analyses were performed by an independent institution, the International Agency for Research on Cancer (IARC), the reliability of the results is assumed to be high.

Furthermore, all time series research and ecological studies that have denied or not shown a positive relationship between PSA screening and a decrease in the mortality rate of prostate cancer were found to have had serious flaws in their research protocols in terms of insufficient duration of follow-up and small differences in the exposure rates of PSA screening among comparable regions, calling their reliability into question.

**Informed Consent for Prostate Cancer Screening**

Controversy may still remain over the effectiveness of screening for prostate cancer using PSA testing for asymptomatic men. However, all reliable studies have revealed a positive correlation between PSA screening and a decrease in the incidence of metastatic prostate cancer as well as the mortality rate for prostate cancer. Therefore, the debate has shifted from the controversy over whether PSA testing decreases mortality rates to the issue of overdiagnosis, overdetection and the effect on QOL following various treatments for screening-detected prostate cancer. Advances in non-invasive treatments maintaining QOL for patients and the development of active surveillance protocols may resolve the uncertainties and controversies concerning the negative impact of PSA screening. The present baseline recommendation for PSA screening is to conduct PSA-screening after shared-informed decision making based on a fact sheet providing updated information on epidemiological features, the merits and demerits of screening and treatment. The Japanese Urological Association will provide fact sheets explaining important issues concerning prostate cancer to men who want to be screened in the near future. Fact sheets are divided into two stages, one is for men who have yet to undergo PSA screening, and the other is for men who have undergone PSA screening. The guidelines on screening for prostate cancer edited by the Japanese Urological Association clearly explain expected outcomes, including both positive and negative impacts, for men undergoing PSA screening and not undergoing PSA screening.

**Policy of the Japanese Urological Association on Screening for Prostate Cancer**

The Japanese Urological Association recommends that 50 years or older undergo PSA screening based on the fact sheets explaining the present status and future outlook for prostate cancer and treatment in Japan as well as the merits and demerits of undergoing screening for prostate cancer, and provides the best available screening system for men who want to be screened.

**Ongoing Study on Screening for Prostate Cancer in Japan**

Two large prospective randomized controlled trials—the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial in the USA and ERSPC in Europe—are now ongoing. However, contamination in control groups may be a serious problem. In contrast, low exposure rates for screening in Japan may be a merit for screening studies in terms of lowering contamination in the control cohort. Therefore, the cluster prospective cohort study, the Japanese Prospective Cohort Study of Screening for Prostate Cancer (JPSPC), was begun in 2001 in order to evaluate the effectiveness of screening for prostate cancer and has been ongoing since 2002. The primary endpoint of JPSPC is comparing changes in the mortality rate for prostate cancer between screening and control cohorts. The JPSPC is prospective cluster cohort study. The screening cohort is municipalities in Hokkaido, Gunma, Hiroshima and Nagasaki prefectures, which have populations of approx. 100,000 in the 50–79 age group. Within the screening cohort, prostate cancer screening campaigns have been
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conducted, and a high exposure rate for screening of 60% or higher over 5 years is expected. Control cohorts are municipalities in the same prefectures with approx. the same sized populations. Aggressive advertising on prostate cancer screening has not been carried out in the control cohorts. In a screening cohort (Ise’saki city), the compliance of PSA screening is high at approx. 75% over 5 years and the number of prostate cancer cases increased rapidly after JPSPS was carried out. In contrast, contamination of prostate cancer screening in a control cohort (Kiryu city) remained low at 8% between 1992 and 2006. In the near future, the changes in the number of metastatic prostate cancer cases in the screening and control cohorts will be announced. Changes in the mortality rate for prostate cancer are to be assessed in 2012.

References