The Radiation Therapy Study Group (RTSG) of the Japan Clinical Oncology Group (JCOG) was established in 2003. The missions of this group are to develop new standards of care with innovative, advanced technology radiation therapy, both for single- and multi-modality cancer treatment, and to improve radiation therapy quality and outcomes of JCOG trials conducted by other organ-oriented groups. In 2004, the first RTSG trial, a Phase II study of stereotactic body radiation therapy for Stage IA non-small cell lung cancer (JCOG 0403), was initiated. Four other trials are currently open for accrual. JCOG 0702 is a Phase I study of stereotactic body radiation therapy in patients with T2N0M0 non-small cell lung cancer. JCOG 0701 is a Phase III study comparing accelerated fractionation with conventional fractionation radiation therapy for T1–2N0M0 glottic cancer. JCOG 0906 is a multicenter safety trial of hypofractionated radiation therapy after breast-conserving surgery in patients with margin-negative invasive breast cancer. JCOG 1015 is a Phase II study of intensity-modulated radiation therapy with chemotherapy for loco-regionally advanced nasopharyngeal cancer. Other RTSG activities include a medical physics working group responsible for dosimetry audits; a genetic analysis working group involved in accompanying research to analyze single-nucleotide polymorphisms to identify predictors of radiation toxicities; a working group that has developed atlases of clinical target volumes for uterine cervical cancer; and participation in the Harmonisation Group to promote global harmonization of radiotherapy and radiotherapy quality assurance among trial groups. Further efforts to improve radiation therapy quality and outcomes of cancer treatment are necessary.

**Key words:** radiation therapy – clinical trials – stereotactic body radiotherapy – intensity-modulated radiotherapy – quality assurance
MD. In 2004, the RTSG opened its first trial, JCOG 0403, a Phase II study of stereotactic body radiation therapy (SBRT) for Stage IA non-small cell lung cancer (NSCLC). This study included a strict quality control and quality assurance program (1), supported in part by the Advanced Technology Consortium (ATC). The digital data of each case from RT planning systems were submitted to the Image-Guided Therapy QA Center (ITC) at Washington University in St Louis, MO, USA, and the final review was performed with the Remote Review Tool provided by the ITC (2). Today, 33 institutions are participating in our five ongoing trials, and the number of accrued patients is now over 600.

ACHIEVEMENTS AND ONGOING TRIALS

JCOG 0403 is a single-arm, Phase II study (3). This study was planned to determine whether SBRT is superior to conventional radiotherapy for patients with medically inoperable cancer and to explore whether SBRT can achieve survival comparable to that with surgery for patients with operable, clinical Stage IA NSCLC. The primary endpoint is 3-year overall survival, and the planned accrual goals are 100 patients with inoperable and 65 patients with operable cancer. Local progression-free survival, patterns of failure and toxicity are included as secondary endpoints. The results for patients with operable cancer were reported at the 52nd annual meeting of the American Society for Radiation Oncology (ASTRO), with encouraging 3-year overall survival of 76% (95% confidence interval, 63–85%), and results for patients with inoperable cancer will be available in 2012 (4).

JCOG 0702 is a Phase I study of the efficacy and safety of SBRT in patients with T2N0M0 NSCLC. The primary endpoint is the incidence of Grade 2 or greater radiation pneumonitis within 180 days after SBRT. This study is employing a continual reassessment method to determine the maximal tolerated dose that will lead to shortening of the accrual period. The results of this study will have a great impact on the determination of the optimal SBRT dose for Stage I NSCLC.

JCOG 0701 is a Phase III study comparing accelerated fractionation with conventional fractionation RT for T1–2N0M0 glottic cancer (5). Conventional fractionation RT consists of 66 Gy in 33 fractions for T1 tumors and 70 Gy in 35 fractions for T2 tumors. Accelerated fractionation RT consists of 60 Gy in 25 fractions for T1 tumors and 64.8 Gy in 27 fractions for T2 tumors. The primary endpoint is 3-year progression-free survival to examine the non-inferiority of accelerated fractionation. The accrual goal is 360 patients, and it will be reached at the end of 2012. In this trial, an accompanying analysis is ongoing to assess single-nucleotide polymorphisms (SNPs) from blood samples to find predictors of radiation toxicities.

JCOG 0906 is a multicenter safety trial of hypofractionated RT after breast-conserving surgery in patients with margin-negative invasive breast cancer. Hypofractionated RT consists of 42.56 Gy in 16 fractions over 22 days for the whole breast. For patients with close margins, boost irradiation of 10.64 Gy in four fractions for 4 days is added. The primary endpoint is the proportion of Grade 2 or greater late adverse reactions at 3 years. When its toxicity proves to be within an acceptable range, hypofractionated RT will be the new standard of care. The accrual goal is 310 patients, and it will be reached in mid-2012.

JCOG 1015 is the most recent trial, a Phase II study of intensity-modulated radiation therapy (IMRT) with chemotherapy for loco-regionally advanced nasopharyngeal cancer. The treatment regimen includes concurrent chemoradiotherapy with two-step IMRT (70 Gy in 35 fractions over 47 days) and three cycles of cisplatin (80 mg/m², day 1, q3w) followed by three cycles of adjuvant chemotherapy with 5-FU (700 mg/m², days 1–5) plus cisplatin (70 mg/m², day 1) repeated every 4 weeks (6). The primary endpoint is 3-year overall survival, and efficacy and toxicity will be analyzed. This trial also has a strict quality control and quality assurance program, including a dosimetry audit, dry-run, and individual case review with the ITC Remote Review Tool.

OTHER ACTIVITIES

JCOG RTSG has working groups (WGs) to tackle issues associated with clinical trials. The Medical Physics WG is responsible for dosimetry audits for SBRT and IMRT trials (7), and its members will serve as consultants when needed. The genetic analysis WG contributed to the development of a JCOG policy for genetic analysis and is now involved in the SNP analysis accompanying JCOG 0701. The Uterine Cervical Cancer WG developed atlases of clinical target volumes for uterine cervical cancer in collaboration with the JCOG Gynecologic Cancer Study Group (8,9). Another WG has started active discussions about future lung SBRT trials in close collaboration with the JCOG Lung Cancer Study Group and the JCOG Lung Cancer Surgical Study Group.

The JCOG RTSG has also supported the JCOG Radiotherapy Committee in the improvement of RT quality and outcomes of trials conducted by other organ-oriented groups. The introduction of RT quality assurance programs in these trials has led to substantial improvements in RT quality (10–12). JCOG is now joining the Harmonisation Group, which aims to promote global harmonization of RT and RT quality assurance among trial groups, including the European Organisation for Research and Treatment of Cancer (EORTC), the Radiation Therapy Oncology Group (RTOG), the Trans Tasman Radiation Oncology Group (TROG), JCOG, the International Atomic Energy Agency (IAEA), the Radiological Physics Center (RPC), the National Cancer Institute (NCI) and the ATC. Continuous efforts to improve quality, especially in advanced technology RT, are mandatory.
CONCLUSIONS

The JCOG RTSG was developed in 2003 and has made substantial achievements through five clinical trials. However, we shall keep trying to improve RT quality and outcomes of cancer treatment. Future research will include multidisciplinary cancer care collaboration with other organ-oriented groups; treatment of intractable cancers; clarification of the effectiveness and reasonable role of highly advanced technology RT, including particle therapy; and more enthusiastically, integration with molecular-targeted therapies.

Acknowledgements

The principal investigators of the JCOG RTSG trials are M.H., MD, Kyoto University (JCOG 0403); Yoshikazu Kagami, MD, Showa University (JCOG 0701, 0906); Hiroki Shirato, MD, Hokkaido University (JCOG 0702); and Yasunasa Nishimura, MD, Kinki University (JCOG1015). Study coordinators are Yasushi Nagata, MD, Hiroshima University (JCOG 0403); Takeshi Kodaira, MD, Aichi Cancer Center and Naoto Shikama, MD, Saitama Medical University (JCOG 0701); Rikiya Onimaru, MD, Dokkyo Medical University and Michihide Mitsumori, MD, Kyoto University (JCOG 0906); and S.I., MD, Nagoya City University (JCOG1015). The members of the JCOG Radiotherapy Committee are Kazushige Hayakawa, MD, Kitasato University; Rikiya Onimaru, MD, Hokkaido University (JCOG 0702); Miwako Nozaki, MD, Dokkyo Medical University and Michihide Mitsumori, MD, Kyoto University (JCOG 0906); and S.I., MD, Nagoya City University; Keiji Nihei, MD, Tokyo Metropolitan Cancer and Infectious Disease Center Komagome Hospital; Takafumi Toita, MD, Ryukyu University; and Y.I., MD, National Cancer Center Hospital. The JCOG RTSG also wishes to thank all of the investigators at its participating institutions for their great collaborative efforts.

Conflict of interest statement

None declared.

References