



NEWSLETTER

Federation of Asian Organization for
Radiation Oncology

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Summer-Autumn
2021



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Greetings

Dear FARO Members,



Greetings!

In behalf of the Philippine Radiation Oncology Society (PROS) Organizing Committee, I would like to invite everyone to the Virtual 5th FARO Meeting, with the theme “Radiation Together for a Stronger Asia”, on October 1 to 3 2021. In line with this we would also like to encourage everyone to submit their abstracts regarding all aspects in the field of Radiation Oncology to be considered for oral or poster presentation, on or before July 30, 2021.

We recognize that these are difficult times for all of us. The pandemic has hit our region hard and there are still many uncertainties ahead of us. Covid has greatly changed our lives and has significantly affected the practice of Radiation Oncology. Yet this should not stop us from doing research and developing improvements in our chosen field, so that our cancer patients will continue receiving the best treatment possible.

That’s why despite the crisis, we strived to give you a comprehensive scientific program involving our very own FARO experts showcasing the best and latest practices and technologies in radiation therapy that Asia has to offer. To learn more about the event and to register, please log on to

<https://meet.faro-asia.org>

We look forward to seeing you in October.

Keep safe everyone.

Sincerely,

Manuel Martin L. Lopez, M.D.
President
PROS

Special Report: ①

Recent Advances in Radiotherapy of Breast Cancer: Hypofractionation and IMRT

Jee Suk Chang¹, Sea-Won Lee²

¹Department of Radiation Oncology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

²Department of Radiation Oncology, Eunpyeong St. Mary's Hospital, Catholic University of Korea College of Medicine, Seoul, Korea

I. Hypofractionation (Figure 1.)

Breast conservation for early-stage breast cancer is one of the most remarkable achievements of modern cancer care. Numerous randomized clinical trials initiated 30 years ago have reported 20-year durable results documenting that survival is equivalent to mastectomy when the breast is conserved with wide excision followed by whole breast radiotherapy (1-7). In the four largest old landmark clinical trials, the whole breast was consistently treated with 50 Gy over 25 fractions. Acute and late toxicities of this conventional treatment was acceptable in most cases; however, the burden of the protracted radiotherapy delivery has been considerable. The desire to reduce the burden of radiotherapy led to investigating alternatives.

Bruce Douglas, a Canadian radiation biologist, first suggested breast cancer might have relatively lower alpha-beta ratio than other malignancies which stimulated the United Kingdom (UK)'s interest and subsequently Canada's interest as well (8). This finding was put to test in clinical trial setting. In Standardisation of Radiotherapy (START) pilot and START A trials, the choice of 13 fractions was derived purely practically. This study design allowed to directly estimate alpha-beta ratio for adverse effects and tumor control by interpolation (9, 10).

Unlike 13 fraction schedules, 3-week 15 fractions regimen designed by Paterson from Manchester led to great success in the START B trial and was adopted as the UK's standard of care in 2009 (11). More than 90% of breast cancer in UK received this regimen until recently. In Canada, 42Gy in 16 fractions was tested in a clinical trial, and with the success of this trial, more than 70% of patients in Ontario received this regimen since 2000 American Society of Clinical Oncology (ASCO) presentation (12). Assuming alpha-beta ratio for late adverse effects, 40 Gy in 15 fractions is equivalent to 45 Gy in 2 Gy fractions. In other words, this regimen is gentler on late-reacting similar and very low loco-regional recurrence rates and toxicity profiles compared with 40 Gy in 15 fractions regimen. Based on this result, UK

normal tissues than 50 Gy conventional fractions with hazard ratio of 0.8 in marked adverse effects reported by the two trials (12, 13).

In a recent survey from 44 European countries, hypofractionation was chosen for whole breast radiotherapy (RT) by 55% and for regional RT by 30%. Interestingly, radiation oncologists working in academic centers or practicing in Western Europe more likely preferred hypofractionation (14). Furthermore, the international expert report was published and endorsed the statement that there is no radiobiological reason why post-mastectomy radiation therapy (PMRT) or regional nodal irradiation (RNI) should have different outcomes to hypofractionation (15).

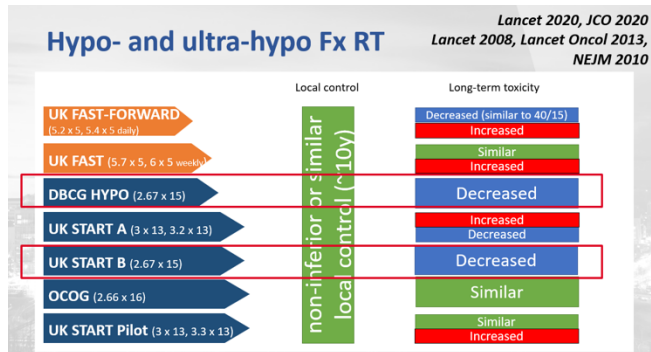
In case of the United States, use of hypofractionation is relatively low but steadily increasing in whole breast RT (16). However, in PMRT/reconstruction or RNI setting, conventional fractionation is still recommended in the National Comprehensive Cancer Network (NCCN) guideline (17). The currently ongoing Alliance trial is recruiting patients to specifically evaluate the impact of hypofractionation in this setting (18).

Last year, there was a Global Breast Cancer Survey study in the pandemic era, and the stark difference between these two societies was evident. When Jennifer Bellon from Massachusetts General Hospital kept saying 1.8 Gy as conventional fractionation, Poortmans, the former president of European Society of Therapeutic Radiation Oncology (ESTRO), responded that it is not conventional, but a historical fractionation. This quote was based on the ultra-hypofractionation, a 5-fraction schedule that approaches the limits of whole breast hypofractionation, which was tested in another two consecutive trials with the long-term safety result of FAST trial and 5-year safety as well as treatment outcome data of FAST-Forward published recently (19, 20). The 5-year efficacy and late normal tissue effect results of FAST-Forward was published in 2020 Lancet and it turns out that 26 Gy delivered in 1 week showed

amended the national consensus to endorse this regimen as standard of care instead of 15 fraction regimens in last October (21). In line with the

expansion of evidence about breast hypofractionation, we at Yonsei have introduced 15

Figure 1. Hypofractionation trials and their results



II. Partial Breast Irradiation (Figure 2.)

In RT omission trials, once observations regarding relapse patterns post breast conservation surgery emerged, investigation began into partial breast irradiation. Because the irradiated volume of breast became smaller, much higher fractional dose would be tolerable and even fewer fractions of treatment can be applicable to selected patients. Building on the lessons learned from 1980's randomized trials of partial breast irradiation (PBI), the next generation was primarily multi-catheter brachytherapy for accelerated partial breast irradiation (APBI), which showed similar local recurrence rates and less late toxicity in APBI (22-29). Then next set of investigations was single-entry balloon brachytherapy device and external beam 3-dimensional conformal RT or intensity modulated radiation therapy (IMRT) APBI. Final results of all these three large phase III randomized trials were published last year in Lancet and Journal of Clinical Oncology. RAPID and National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39 trials which included several thousand cases showed successful results despite some caveats (27, 30). APBI-IMRT-Florence trial was most impressive, a practice changing trial that 30 Gy in 5 fraction to partial breast in every other day using IMRT showed similar local control rate while decreased toxicity and better cosmesis than conventional whole breast RT (31).

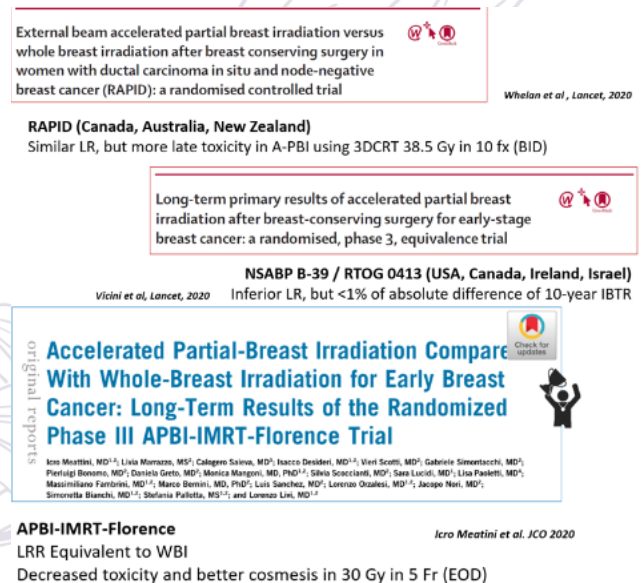
Over the last three decades, various techniques have been introduced with promising clinical outcomes. However, because of relatively small breast volume in Asian women, most radiation oncologists in Korea felt uncomfortable to apply

fraction regimen in the early 2010's and 5 fraction schedule last year.

APBI with conventional techniques. Gangnam Severance is one of the top accrual hospital of Targit intraoperative RT trial in the world, and I still feel uncomfortable to see applying applicator to small sized breast.

Among various options, Yonsei Cancer Center implements Cyberknife based stereotactic-partial breast irradiation (S-PBI) in highly selected women with 30 Gy in 5 fractions in every other day. The preliminary result was published in 2020 (32). We observed almost no skin reaction within 1-year after S-PBI and considering that skin thickness is known for its relationship with palpable induration, we observed the change in skin thickness with follow-up ultrasound exams, which in PBI appears to be limited to the tumor bed, in contrast to the diffuse skin thickening observed after whole breast RT. In our daily practice, 15 fractions regimen are still the most popular schedule and 5 fractions whole breast or partial breast is cautiously used in 2 out of 10 patients at Yonsei.

Figure 2. Partial breast irradiation trials and their results



III. Intensity Modulated Radiation Therapy (Figure 3.)

Comprehensive loco-regional radiation was proven in high-risk patients in old clinical trials, and subsequently proven even in early-stage patients with high-risk features (33-37). In 2015, first high-level evidence was published support including the internal mammary nodal (IMN) chain in RT field.

However, at the same time, it seems clearer that radiation exposure to heart inevitably increases subsequent cardiac disease as Darby first reported in 2013 (38), even in modern data in 2017 (39), and our group also reproduced identical results in Korean population (40).

In Yonsei, we have adopted all available devices or techniques for maximal heart sparing as possible. Deep inspiration breath hold (DIBH) with Abches in 2013, IMRT and prone in 2015 and continuous positive airway pressure (CPAP) in 2020.

With advent of systemic agents and screening program, long-term survivors have become more common (41). Accordingly, radiation related toxicity is becoming more and more important for patient care. Volume based and individualized treatment planning is the way to go in modern radiotherapy. Whatever the reason, use of IMRT is increasing over time, and especially in breast cancer. However, in contrast to head and neck cancer and lung cancer, target volume contouring methods for breast cancer are still mostly based on conventional field based and 2 dimensional RT techniques. International expert consensus recommend modern breast RT should be based on anatomical definitions of target volumes (42).

Considering actual loco-regional recurrence risk, we previously conducted target volume validation studies and suggested that ESTRO clinical target volume (CTV) was sufficient to cover early stage cases while in higher nodal stage cases, individual modification may be necessary (43, 44). However, according to a Korean multicenter dummy run study, there are extremely large variations in target volume delineation and planning results among physicians and hospitals (45). For example, in a same patient, mean heart dose (MHD) and lung V20% had huge inter-hospital variation from 3 Gy to 24 Gy, and 5% to 60%. We also showed that IMRT experience matters and MHD below 2 Gy can be achieved with 2 partial arc-based volumetric modulated arc therapy (VMAT) plan when combined with CPAP-based respiratory motion control, is as good as proton beam therapy.

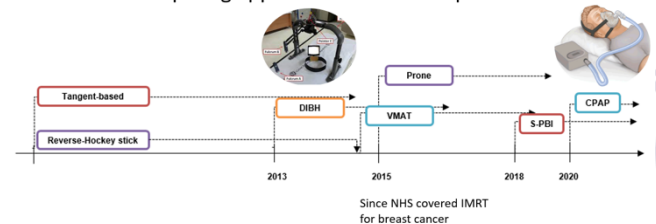
IV. Conclusion

In conclusion, de-escalation strategies such as hypofractionation, ultra-hypofractionation, and PBI as well as use of cardiac-sparing technique are becoming more and more important in modern oncology. IMRT varies in sophistication and there are wide inter-hospital discrepancies in dose-

volume profiles. In breast IMRT, quality assurance schemes for RT target and plans are becoming more important.

Figure 3. Treatment strategy at Yonsei

- Comprehensive RNI including IMN is routinely considered
- Maximal heart sparing approach has been adopted



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Special Report: ②

Organ preservation with radical radiotherapy in muscle invasive bladder cancer:

Recent Advances and Future Prospects

Speaker: Dr Nuradh Joseph (Sri Lanka)

There is robust data to suggest that radical radiotherapy is equivalent to radical cystectomy in patients with localised muscle-invasive bladder cancer (MIBC) (1). In contrast to surgery, radiotherapy offers an opportunity at organ preservation and has less treatment related morbidity and mortality. However, utilization of radiotherapy in this setting is low, due to percepts that radical cystectomy remains the “gold-standard”. Two large randomised controlled trials (BCON and BC2001) conducted in the United Kingdom, showed that radiosensitisation with either the hypoxia modifier Carbogen and Nicotinamide (CON) or a 5-fluorouracil and mitomycin based chemotherapy regimen, improves survival compared to radiotherapy alone (2,3).

In this webinar, we reviewed the evidence supporting the clinical equipoise of radical radiotherapy with radical cystectomy in localised MIBC and revisited the trials of radiosensitization. Subsequently, the following three recent updates of these two trials were discussed in detail:

- The Meta-analysis of the BCON and BC2001 by Choudhury et al which showed superiority with hypofractionation (55 Gy in 20 fractions over 4 weeks) in comparison to conventional fractionation (64 Gy in 32 fractions over 6.5 weeks) (4).
- Long term outcomes with biomarker stratification in the BCON trial by Song et al which validated necrosis and an mRNA based hypoxia gene expression signature as robust predictive biomarkers of benefit with hypoxia modification (5).
- Outcomes in patients treated with neoadjuvant chemotherapy followed by chemoradiotherapy in the BC2001 trial by Hussain et al. which confirmed the benefit

of radiosensitising chemotherapy even in patients treated with neoadjuvant chemotherapy (6).

Finally, we discussed current studies and future prospects in the space of bladder preservation in MIBC as listed below:

- Tumour focused radiotherapy and whole bladder sparing approaches
- Adaptive radiotherapy
- Personalised fractionation regimens
- Combining hypoxia modification and radiosensitising chemotherapy

The panel discussion addressed a large number of questions from the participants with particular focus on implementation of hypoxia modification as a cost-effective easily deliverable strategy of radiosensitization, especially in our region.

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THE 6TH FARO WEBINAR RECENT ADVANCES IN RADIOTHERAPY OF BREAST CANCER: HYPOFRACTIONATION AND IMRT THURSDAY, MAY 27 2021

FARO WEBINAR SERIES



THE 7TH FARO WEBINAR ORGAN PRESERVATION WITH RADICAL RADIOTHERAPY IN MUSCLE INVASIVE BLADDER CANCER: RECENT ADVANCES AND FUTURE PROSPECTS

FARO WEBINAR SERIES

TUESDAY, 22 JUNE 2021



Greetings from Member Organization

Philippine Radiation Oncology Society (PROS) Profile

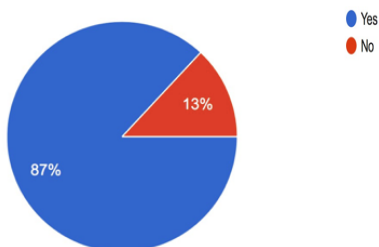


The Philippine Radiation Oncology Society (PROS), a subspecialty society of the Philippine College of Radiology (PCR), was formally organized in 1988. PROS has 106 active members to date across 49 radiotherapy facilities in the entire archipelago.

As the country faces the COVID-19 surge due to Delta variant, preliminary results of a recent survey showed that a majority (87%) of respondents have adopted hypofractionation at some point in their practice. Adequate data and the pandemic itself are top 2 reasons to treat breast and genitourinary cancer sites using moderate hypofractionation (2.7-3 Gy fraction size).

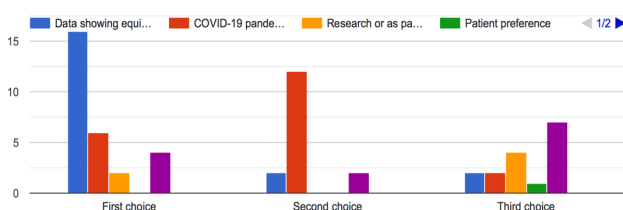
1) Have you adapted hypofractionated radiation therapy regimens/protocols in your practice?

23 responses



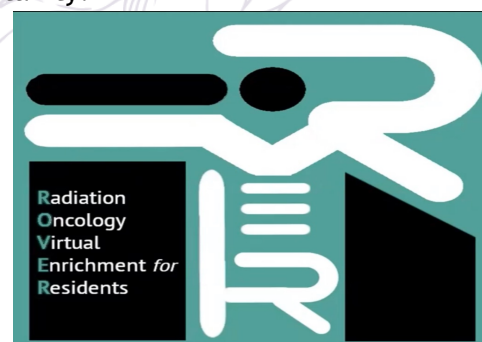
PROS Residency Training Council (RTC) and Committee on Research have quickly adapted digital platform when the scientific meeting held last July 2020 was successfully hosted by Jose R. Reyes Memorial Medical center together with online or web-based in-service exam. The Residents' Research Forum (descriptive category) was also conducted virtually on October 2020.

2) What are the top three (3) reasons for adopting hypofractionation in your practice? (Please rank as first, second, or third choice)



A total of 12 case reports were submitted using pdf format and uploaded in a shared drive. Preliminary judging for top 3 posters a few days prior was done by all active consultants through online poll. The chosen case reports for 10-minute oral presentations were orbital chondrosarcoma, conjunctival lymphoma and neuroendocrine cancer of the uterine cervix with 97 online participants.

As the pandemic evolves, RTC continues to think of ways to maximize learning through the introduction of Radiation Oncology Virtual Enrichment for Residents (ROVER) among its 50 residents-in-training across nine training hospitals. A triad of consultants are invited as lecturer, reactor and facilitator of contouring activity. A short post-quiz follows and the first one who gets a perfect score upon online submission will win a prize (gamification) as initiated by the PCR President herself, Dr. Maria Lourdes Lacanilao. This is a means of "Recognizing their hard work" as the Philippine Council for Mental Health through the Department of Health strongly recommends it. Indeed, *no one is left behind* in this time of great uncertainty.



UPCOMING EVENTS

EVENTS	DATE	CONGRESS VENUE	HOMEPAGE
The 5th FARO Meeting “Radiating Together for Stronger Asia”	1-3 October 2021	Virtual	https://meet.faro-asia.org
FARO Webinar “Hippocampal avoidance-WBRT + Memantine vs SRS in Brain Metastasis/ SBRT in Oligometastasis”	November 2021	Virtual	Hosted by THASTRO https://www.thastro.org/en/
FARO Webinar “SBRT in Liver”	December 2021	Virtual	Hosted by MOSTRO



Virtual 5th FARO Meeting

Hosted by the **Philippine Radiation Oncology Society**

October 1-3, 2021

<https://meet.faro-asia.org>

FARO MEMBERS ORGANIZATIONS

		Bangladesh Bangladesh Society of Radiation Oncologists (BSRO) http://www.bsro.info/			Mongolia Mongolian Society for Radiation Oncology (MOSTRO)
		China Chinese Society of Therapeutic Radiation Oncology (CSTRO) http://www.csro.org/			Myanmar Myanmar Society for Radiation Oncology (MSTRO) https://www.mmcentral.org/societies/myanmar-society-for-radiotherapy-oncology/
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		Korea Korean Society for Radiation Oncology (KOSRO) https://eng.kosro.or.kr			Sri Lanka The Sri Lanka College of Oncologists (SLCO) http://slco.lk/
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