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S.A. KOPOCHKINA[1], A.D. SAVKHATOVA[2], M.D. ZEKEBAEV[2], D.E. CHEN[1], E.R. DAVLETGILDEYEV[1]

[1]НАО «Казахский национальный медицинский университет им. С.Д. Асфендиярова», Алматы, Республика Казахстан;
[2]АО «Казахский научно-исследовательский институт онкологии и радиологии», Алматы, Республика Казахстан

Intensification of radiation therapy for localized breast cancer in the settings of the COVID-19 pandemic: A literature review

Relevance: *Since 2004, breast cancer steadily ranks first in the structure of the incidence of malignant neoplasms in the Republic of Kazakhstan in both sexes. In 2020, its share was 14.5% (vs. 15.2% in 2019). Breast cancer also constantly ranks first in the structure of female cancer incidence, with 44.3‰ in 2020 (vs. 51.6‰ in 2019). In the early 1980s, radiation therapy was a standard specialized treatment for breast cancer. The current realities of the COVID-19 pandemic require a reorganization of healthcare facilities to determine the priorities. It is also important to balance the economic and clinical efficacy of radiotherapy methods applied.*

The study aimed to *analyze the results of large randomized trials and compare breast cancer outcomes after hypofractionated and standard fractionation radiation treatment.*

Methods: *We reviewed the results of large randomized trials of hypofractionated radiation therapy, emphasizing good patient selection according to the American Society of Therapeutic Radiology and Oncology (ASTRO) guidelines. Radiobiological aspects of hypofractionation were considered due to its implementation in clinical practice. The research materials were obtained from the "PubMed" database of evidence-based medicine by the keywords "radiotherapy," "breast cancer," "hypofractionation dose" for the period of 2000-2021. Large randomized trials involving patients of any age diagnosed with stages T1-3, N0-1 breast cancer, who underwent beam therapy in standard or hypofractionated mode, met the criteria for inclusion in this study.*

Results: *According to the results of large randomized trials, the hypofractionated regimen is similar to the standard regimen in terms of late effects on normal tissues and ensures reasonable control over the oncological process.*

Conclusions: *Hypofractionation has proven effectiveness and safety and lower late and acute radiation toxicity when treating early breast cancer. Hypofractionation can become a new standard of radiation therapy at early stages after breast-conserving surgery.*

Keywords: *radiotherapy, breast cancer, dose hypofractionation.*

Introduction: The effectiveness of radiation therapy in breast cancer (BC) was proved in many randomized trials (one of the first trials – NSABP B-06 – was published in 1985). Radiation therapy was recognized as the standard for breast cancer in the early 1980s.

Since then, the radiation therapy methods have been improved annually. Today's primary guideline for development in the treatment process arrangement is determining a practical, economically accessible, and patient-friendly radiation therapy method.

Breast cancer ranks first in the structure of malignant neoplasms in both sexes with a specific weight of 14.5% (in 2019 – 15.2%) in the Republic of Kazakhstan (RK) under statistics data. This situation has been stable since 2004. Besides, breast cancer is in the first place and constantly occupies this position in the structure of female oncopathology – 44,3‰ (in 2019 – 51,6‰) [1]. Unfortunately, the number of patients requiring radiation therapy grows every year.

Radiation using a 50 Gr regimen for 25 fractions within five weeks was recognized as the standard treatment for breast cancer after breast-conserving surgery. Early studies have shown that this combination of surgical treatment and adjuvant radiation therapy is as effective as mastectomy [2, 3]. The support of standard fractionation (SF) during irradiation of the entire breast in BC is based on the radiobiological consideration that radiation damage to normal tissue is more voluminous at a large dose per fraction without additional radiation to the tumor [4]. However, SF's problems are cost and discomfort for patients who undergo sessions every day for 5-7 weeks.

Tissues in the human body respond differently to radiation therapy, thus falling into two categories: acutely responsive tissues with poor repair capacity and tissues that respond late and have a high repair capacity. The α/β ratio (sensitivity to fractionation, or ability to recover) corresponds to a parameter that the number of dying cells, react-

ing early and reacting late, is the same. It shows the curvature of the cell survival graph in the form of a linear-quadratic concept that can predict the response of these two types of tissues [5]. The mammary gland is more sensitive to high-dose fractionation because this type of tumor has a low α/β ratio (α/β=4). So, an adequate radiation therapy regimen can be prescribed without increasing the incidence of late toxicity in normal tissues.

The study aimed to analyze the results of large randomized trials and compare breast cancer outcomes after hypofractionated and standard fractionation radiation treatment.

Materials and methods: In this literature review, we studied the results of pivotal randomized trials of HF radiation therapy, emphasizing good patient selection according to the American Society of Therapeutic Radiology and Oncology (ASTRO) guidelines of 2011 [6] and 2018 [7] considering radiobiological aspects of hypofractionation due to its implementation in clinical practice. The research materials were obtained from the "PubMed" database of evidence-based medicine by the keywords "radiotherapy," "breast cancer," "hypofractionation dose" for the period of 2000-2021. Large randomized trials involving patients of any age diagnosed with stages T1-3, N0-1 breast cancer, who underwent beam therapy in standard or HF mode, met the criteria for inclusion in this study. We also considered the National Comprehensive Cancer Network (NCCN) of 2021 [8].

Results:

Key randomized trials

As of today, four randomized trials - Trial conducted by the Royal Marsden Hospital/Gloucestershire Cancer Center (RMH/GOC) [9, 10], Standardisation of Breast Radiotherapy (START) A and B trial conducted in the UK [11-13] and the Canadian study [14] – have published 10-years observation results that support the idea of efficient hypofractionation. Table 1 provides details of the study design, enrollment criteria, fractionation mode, and treatment outcomes. All trials involved patients with early breast cancer stages T1-3, N0-1. Most patients were above 50 years. Some received chemotherapy; some were exposed to regional lymph node irradiation or boost tumor irradiation. The Canadian study did not involve patients who underwent regional lymph node irradiation or additional tumor bed irradiation, although other studies allowed such patients.

Table 1 – Characteristics of the study population and conclusions of the main randomized trials on hypofractionated total breast irradiation

Characteristics	RMH/GOC			START A			START B		Canadian study	
No. of patients	1 410			2 236			2 215		1 234	
Age, <50 years (%)	30.3			23			21		25	
Stage	T1-3/N0-1			pT1-3aN0-1			pT1-3aN0-1		pT1-2N0	
pNO (%)	40			69			74		100	
Stage 3 (%)	-			28			23		19	
Lumpectomy (%)	100			85			92		100	
Chemotherapy (%)	13.9			35			22		11	
RLNI (%)	21			14			7		0	
Boost tumour irradiation (%)	75 (14 Gr/7 Fr.)			61 (10 Gr/5 Fr.)			39 (10 Gr/5 Fr.)		0	
Dose/ fraction	50 Gr/25 Fr.	39 Gr/13 Fr.	42.9 Gr/13 Fr.	50 Gr/25 Fr.	39 Gr/13 Fr.	41.6 Gr/13 Fr.	50 Gr/25 Fr.	40 Gr/15 Fr.	50 Gr/25 Fr.	42.5 Gr/16 Fr.
EQD2 of the tumour (Gr, α/β = 3.5)	50.0	46.1	53.0	50.0	46.1	50.7	50.0	44.8	50.0	47.6
EQD2 of the breast (Gr, α/β = 3.1)	50.0	46.6	53.8	50.0	46.6	51.4	50.0	45.2	50.0	48.0
Local control	RIBT, 10 years (%)			LRR, 10 years (%)			LRR, 10 years (%)		LR, 10 years (%)	
	12.1	14.8	9.6	7.4	8.8	6.3	5.5	4.3	6.7	6.2
Normal tissue toxicity	Any changes in the appearance of the breasts within 5 years (%)			Breast induration Telangiectasia Breast edema			Breast reduction Telangiectasia Breast edema		Good or excellent cosmetic effect (%)	
	39.6	30.3	45.7	39 Gr better than 50 Gr			40 Gr are pre-ferred		71.3	69.8

Notes: RLNI – regional lymph node irradiation; Fr. – fraction; RIBT – recurrent ipsilateral breast tumor; LRR – locoregional relapse; LR – local relapse.

The RMH/GOC experimental study determined α/β of the breast tissue; late toxic effects from normal tissues were the primary endpoint. In the study, two different HF modes of 13 fractions of 39 Gr or 42.9 Gr within five weeks were compared with a standard scheme of 50 Gr in 25 fractions. Comparison of the three modes allowed the α/β to be estimated for several endpoints associated with irradiation by assuming linearity between the two trial dose levels. An interpolation could determine a schedule of 13 fractions effective at 50 Gr in 25 fractions. After a minimum of 9.7 years of observation, various changes in the appearance of the breasts were observed in 39.6%, 30.3%, and 45.7% of patients; recurrent ipsilateral breast tumors occurred in 12.1%, 14.8%, and 9.6% of patients exposed to 50 Gr/25 fractions, 39 Gr/13 fractions, or 42.9 Gr/13 fractions of irradiation, respectively [9]. Based on these results, α/β for breast cancer was similarly assessed as 4.0 Gr, as in the case of healthy tissue with a late reaction [10]. Since the 42.9 Gr in 13 fractions mode caused a late toxic response in normal tissue compared to SF [11], the START A study compared the 39 Gr and 41.6 Gr in 13 fractions mode within five weeks with SF mode. Notably, both HF and SF treatment took five weeks in the RMH/GOC and START A studies meaning that the patients received no standard treatment.

The START A study revealed no significant differences between the HF groups (39 Gr or 41.6 Gr) and the control SF group over ten years of observation. Disease-free survival and overall survival did not differ significantly between any treatment regimens. Besides, moderate to severe breast induration, telangiectasia, and breast edema were less common effects of normal tissues in the 39 Gr group compared to the 50 Gr group [13].

The START B study aimed to provide a robust evidence base for clinical applications of breast radiotherapy by comparing the widely used HF program 40 Gr/15 fractions within three weeks with SF. The first endpoint of locoregional relapse revealed no difference between the two treatment groups. Late reactions of normal tissues like breast reduction, telangiectasia, or breast edema were much less frequent in the HF group than in the SF group [13].

Finally, the Canadian study compared the HF regimens of 42.5 Gr in 16 fractions with SF. After ten years, there were no differences in the number of cumulative local relapses between the two fractionation regimens [14]. Local relapse occurred in 6.7% of cases in the SF group vs. 6.2% in the HF group. Regarding the cosmetic effect, 71.3% of patients in the SF group and 69.8% in the HF group had a good or excellent decorative effect with no statistically significant differences.

ASTRO recommendations

Initial trial reports confirmed the safety and efficacy of HF. In response, in 2011, the American Society for Therapeutic Radiology and Oncology (ASTRO) published the evidence-based dose fractionation guidelines for breast radiotherapy [6]. The Guidelines state that the Group has reached a consensus regarding HF administration to patients meeting all of the following criteria: age above 50 years, the disease stage T1-2N0, no previous chemotherapy, and the central axis dose from 93% to 107%. Recommended fractionation schemes: 42.5 Gr in 16 fractions as in the Canadian study, 41.6 Gr in 13 fractions within five weeks as in START A, or 40 Gr in 15 fractions within three weeks as in START B. The HF doses used in the RMH/GOC trial compared to the 50 Gr group were not recommended since the 42.9 Gr group produced excessive toxicity. The 39 Gr group showed a higher risk of developing an ipsilateral breast tumor. These recommendations are pretty conservative. The Guidelines say that, regarding other patients, the workgroup could agree neither for nor against the use of the HF. However, this should not be interpreted as a contraindication to its use [6].

Although there has been a significant increase in evidence favoring HF since then, its use remained low in patients meeting the criteria [15-17]. According to the studies, practicing radiologists and oncologists made nearly three-fourths of relevant decisions, not patients [18]. This brought to life new evidence-based guidelines published by ASTRO in 2018 after collecting even more new results from various randomized trials and comparing them with the available data [7]. The new ASTRO guidelines include recommendations about fractionating the radiation dose and planning and implementing treatment. This is expected to reduce the variety of treatment options and increase individual decision-making approaches based on various tumor factors, anatomical features, and patient preferences. Table 2 compares the HF eligibility criteria in ASTRO recommendations of 2011 and 2018.

Table 2 – Patients for whom the Consensus supports the use of hypofractionated whole-breast irradiation: the comparison of ASTRO recommendations of 2011 and 2018

Factor	2011 guidelines	2018 guidelines
Age	≥50 years	Any age
Disease stage	T1-2N0	Any disease stage is subject to the intention to heal the entire breast without additional field to cover regional lymph nodes
Chemotherapy	No	Any chemotherapy
Dose uniformity	±7% over the central axis	Breast tissue volume receiving 105% of the pre-scribed dose shall be minimized regardless of the dose fractionation

Thus, HF up to a dose of 40 Gr in 15 fractions or 42.5 Gr in 16 fractions is a preferred fractionation scheme for women with invasive breast cancer undergoing radiation therapy of the breast with or without the armpit region corresponding to the 1st lymph node level. A consensus was reached regarding additional irradiation of the tumor bed in patients with invasive breast cancer meeting any of the following criteria: any stage of cancer at the age below 50 years; advanced cancer or positive resection margins at the age of 51 to 70 years. Additional irradiation of the tumor bed can be administered to patients with ductal carcinoma in situ, meeting any of the following criteria: age below 50 years, positive or close to positive (<2 mm) margins. In other cases, the decision is highly dependent on the patient's preferences and values. When planning the intervention, breast tissue volume receiving 105% of the prescribed dose shall be minimized, and the tumor bed delineated to receive at least 95% of the specified amount. The quantity to the heart, contralateral chest, lungs, and other normal tissues should be minimal.

It is worth noting that the Guidelines encourage appropriately individualized collaborative decision-making by doctors and patients. Nothing should be construed as strict or overriding individual physicians and patients' properly informed and balanced judgments. Therefore, the working group does not recommend the use of any quality criteria that require a 100% use of HF even in patients with absolute indications for HF, as the distribution of reasonable values and patient preferences can be expected to result in the patient-centered choice of conditional fractionation in a particular proportion of patients.

Indications except for recommendations

1. Age.

Young age is a risk factor for the development of local BC [19]. However, only 21-30% of patients were under 50 in crucial dose hypofractionation (HF) randomized trials. A subgroup analysis in the Canadian study showed that the effect of the fractionation scheme on the development of ipsilateral breast tumors did not differ regardless of age. Moreover, younger patients preferred HF in terms of local-regional recurrence in the 10-year results of the START trial published after the ASTRO recommendations [13]. It justifies the dose HF effects for patients under 50 years of age.

2. Ductal carcinoma in situ (DCIS).

DCIS patients were not included in the main trials. However, a randomized study is now going on [20] to confirm the efficacy and safety of dose HF in patients with DCIS. Besides, many retrospective data and meta-analyses show no differences in local recurrence between HF and SF [21, 22]. In DCIS, HF is unlikely to deteriorate tumor control or exacerbate side effects compared with SF [23]. Therefore, patients may be offered dose HF as an alternative.

3. Disease degree.

Subgroup analysis in the Canadian study showed that dose HF was less effective for high-malignant tumors than for low-malignant tumors [14]. However, the results of the 10-year follow-up in START A and B trials did not show that the treatment effect was significantly different depending on the severity [13]. It can be explained that additional irradiation of the tumor bed in the Canadian study was not allowed. At the same time, 61% and 39% of patients underwent additional irradiation of the tumor bed at 10 Gr/5 fractions, respectively, in START A and B trials. Another explanation is that the Canadian study initially used the Scharf-Bloom-Richardson (SBR) rating system. The more successful Nottingham grading system has superseded this system. When the results were assessed using the Nottingham rating system, no association was found between the tumor stage and the radiation therapy received for local recurrence [24]. Moreover, a population-based cohort study shows no adverse HF outcomes in patients with stage III breast cancer [25].

4. Irradiation of regional lymph nodes.

Only 21%, 14%, 7%, and 0% of patients have received regional nodal irradiation in the RMH/GOC, START A, START B trials, and Canadian study. Although only one of 750 patients in the 41.6 Gr/13 fractions group in START A developed brachial plexopathy [11], there was no significant difference in shoulder mobility or hand edema between the HF and SF groups in START A and B [13]. Follow-up after HF irradiation of the entire breast in both START trials was insufficient to exclude such late toxicity. However, several retrospective data supported the use of HF for irradiation of regional lymph nodes. Based on a literature review by Galecki et al. [26], the risk of brachial plexopathy due to radiation was less than 1% when using dosing regimens per fraction from 2.2 to 2.5 Gr with a total boost dose of 34-40 Gr Published data now support the feasibility of HF radiotherapy of regional lymph nodes and the need for a prospective randomized study of clinical outcomes and toxicity relative to SF [27]. According to the 2021 NCCN guidelines, the radiation dose should be 45-50.4 Gr/25-28 fractions to the areas of regional lymph nodes [8]. Additional irradiation of the regional lymph nodes can be performed to irradiate those lymph nodes that are severely affected or enlarged (internal mammary or clavicular lymph nodes) and have not undergone surgery.

5. Chemotherapy.

From 11% to 35% of patients received chemotherapy in pivotal randomized trials. Chemotherapy regimens containing anthracycline and taxane were used in 25% and 1% of patients in the START A trial and 13% and 0.4% of patients in the START B trial, respectively [11, 12]. Cardiac toxicity is a significant concern with anthracycline chemotherapy. Risk indicators of toxicity in normal tissues did not differ significantly regardless of the use of chemotherapy when the results of the Canadian study and the START A and B trials were analyzed [13, 14]. Although the current follow-up data is relatively short given late cardiac toxicity, the radiological review of HF that will be discussed in more detail later, as well as existing radiation delivery methods such as intensity-modulated radiation therapy (IMRT), can save a significant amount of radiation dose received by the heart.

6. Additional irradiation of the tumor bed (boost).

Regarding additional radiation of the tumor bed, 75% of patients received 14 Gr in 7 fractions in the RMH/GOC studies, and 61% and 39% - 10 Gr in 5 fractions in START A and B trials, respectively, while no additional irradiation of the tumor bed was performed in the Canadian study. The ASTRO guidelines state: "The working group recognized that it is inappropriate to use only HF (without additional radiation) when it is assumed that additional radiation of the tumor bed is indicated. The optimal dosing regimen for the use of additional radiation in combination with HF has not been determined." However, meta-analyzes of RMH/GOC, START A, and START B showed that the groups using HF showed significantly better results regardless of additional radiation of the tumor bed with moderate to severe side effects from normal chest tissue assessed by a physician. It is noteworthy that the ASTRO manual was published in 2011 before these most recent data were obtained [13]. Kim et al. [28] reported the results of a Phase II HF study as 39 Gr/13 fractions of 3 Gr per the whole breast once a day during five consecutive working days, and 9 Gr/3 successive fractions of 3 Gr per area after lumpectomy, total duration 3.2 weeks. They reported excellent disease control and moderately tolerated skin toxicity in patients with early breast cancer. The 2021 NCCN guidelines state that "additional irradiation of the tumor bed is recommended for patients at high risk of recurrence. Typical boost dosage regimens are 10-16 Gr/4-8 fractions" [8].

Radiobiological explanation

The radiobiological rationale for HF is based on the idea that if α/β of a tumor is equivalent to α/β of normal tissue exposed to radiation, then fractions with a high dose of radiation will be more effective without harming normal breast tissue.

As mentioned before, an important advance in the RMH/GOC and START A trials was the ability to assess the susceptibility to fractionation; α/β of the breast tumor and normal tissue. These values can vary depending on the measurement results and the time of observation, as indicated in Table 3. In addition to RMH/GOC, Yarnold et al. [9] reported that α/β was equal to 4.0 for local control and 3.6 for side effects. After five years of START A trial, the RMH/GOC and START A meta-analyzes showed that the adjusted estimates of α/β values were equal to 4.6 Gr for tumor control and 3.4 Gr for late changes in breast appearance (photographically) [11]. Finally, a meta-analysis of the RMH/GOC and START A trials in 10 years of results from the START study gave an adjusted α/β value of 3.5 Gr for locoregional recurrence [13] and 3.1 Gr for side effects [29].

Table 3 – α/β (Gr) assessment in RMH/GOC and START A trials

Results	RMH/GOC (10 years)		RMH/GOC and START A meta-analysis (5 years)		START A (10 years)		RMH/GOC and START A meta-analysis (10 years)	
LR or LRR	4.0		4.1 (4.6)		4.0 (adjusted)		3.5	
Normal tissue toxicity	The appearance of the breasts (any changes) Breast reduction Breast induration Telangiectasia Breast edema	3.6 4.7 3.1 5.1 2.3	The appearance of the breasts (any changes)	3.6 (3.4)	Breast reduction Breast induration Telangiectasia Breast edema	3.5	Side effects (see Yarnold et al. [29])	3.1

Notes: LRR – locoregional relapse; LR – local regression.

Another critical aspect of the effect of HF is that the total radiation dose in HF, calculated in EQD2, is slightly less than for SF. Yarnold et al. [30] noted that the standard tissue toxicity curve in the dose-response plot should be steeper than the subclinical breast tumor control curve, assuming that local control would be about 70% without radiation exposure toxicity from normal tissues would be zero without the use of radiation. As a result, it slightly decreases the total dose and enables a significant reduction in normal tissue toxicity with good stabilization of local control (Figure 1).

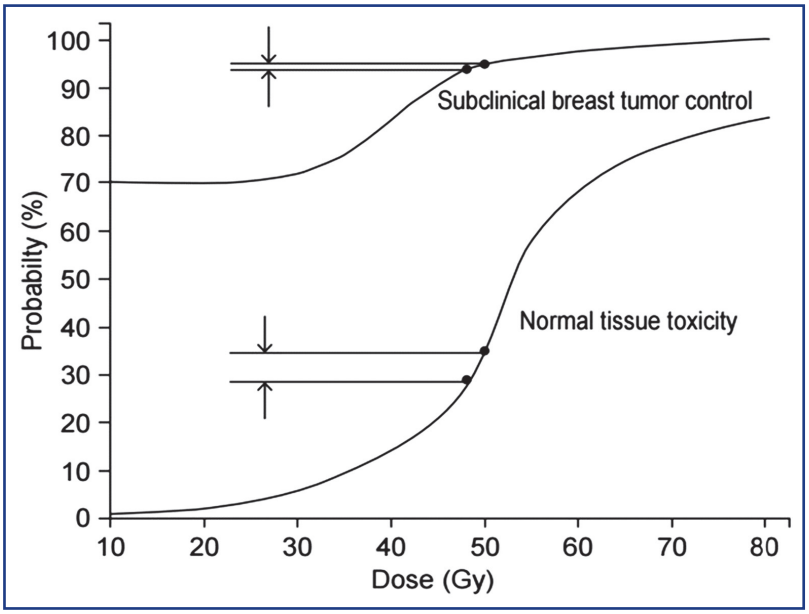

Figure 1 – Dose-response for the subclinical breast tumor control and normal tissue toxicity [30]

The main problem with high doses per fraction is cardiotoxicity. Contrary to popular belief about the detrimental effect of HF on the heart, it is worth remembering that EQD2 in HF mode is softer for the heart than in SF mode, even if we consider α/β of the heart as an extreme value (α/β = 1). With the HF mode of the Canadian study (42.5 Gr/16 fractions), the average dose of EQD2 for the heart is less critical than with the SF [31].

While critical studies have focused on detecting late normal tissue reactions to high doses per fraction, reports have been published regarding acute responses due to the use of the HF regimen [32–34]. Since the total HF dose is slightly lower than the usual irradiation regime, a significant reduction in acute skin reaction is expected, given the higher α/β value for critical skin reaction. As expected, Jagsi et al. [33] reported that patients treated with HF had a lower skin response as rated by a physician, and patient-reported pain, burning, swelling, and fatigue. Shaitelman et al. [34] also reported a decrease in acute toxicity and improved patients' quality of life with subsequent HF. These studies confirm that HF provides patients with greater comfort (due to a shorter treatment program) and reduces the incidence of acute dermatitis and pain, ultimately improving their quality of life.

Discussion:

Further study of the issue

The effectiveness and safety of the HF regime use are still widely studied. The SUPREMO study is an open, international, randomized controlled tri-

al investigating the effects of different radiation therapy regimens after mastectomy [35]. Women in the age of 18 years and older with intermediate-risk breast cancer (defined as pT1-2N1; pT3N0; or pT2N0, also stage III or with lymphovascular invasion) who underwent a mastectomy and, in the presence of positive lymph nodes, armpit surgery, randomly distributed (1:1), received chest radiation therapy (50 Gr/25 fractions or a radiobiologically equivalent dose of 45 Gr/20 fractions or 40 Gr/15 fractions) or were without radiation therapy. Interim data showed that radiation therapy after breast removal resulted in more local (chest) symptoms within two years after randomization compared with no radiation therapy, but there was little difference between groups. These data will be used to make general decisions while waiting for survival outcomes (primary endpoint of the study).

Consideration of post-mastectomy radiation therapy

Under the available data, postmastectomy HF is not inferior to SF and has similar toxicity in high-risk breast cancer patients with short-term follow-up. A meta-analysis and systematic review by Liu et al. [36] included 25 clinical trials involving 3871 patients after mastectomy with breast cancer. They concluded that HF radiation did not significantly differ in efficacy and toxicity in this patient population compared to conventional radiation therapy, highlighting the need for more extensive randomized controlled trials. However, HF safety data in patients with breast reconstruction remain limited. Ideally, HF is expected to minimize complications without compromising appearance. It is essential to understand the relationship between the radiation therapy regimen and the reconstruction results as breast reconstruction progresses. The Alliance A221505 study (RT CHARM: a phase III randomized trial of HF irradiation after mastectomy with breast reconstruction) is currently underway, and it investigates clinical cases of patients who underwent mastectomy with immediate or delayed reconstruction and subsequently received HF (42.56 Gr/16 fractions) or SF (50 Gr/25 fractions).

Conclusions: Hypofractionation has proven effectiveness and safety and lower late and acute radiation toxicity when treating early breast cancer. Today, the COVID-19 pandemics pose the main burden on the healthcare system, considering the HF regimen is very relevant since this method of radiation therapy is more comfortable for patients and much more economical. However, the lack of specific data on this issue requires further studies of the economic efficiency of this method for a more accurate picture. We believe that hypofractionation can become a new standard of radiation therapy at early stages after breast-conserving surgery.

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ТҰЖЫРЫМ

С.А. Копочкина[1], А.Д. Савхатова[2], М.Д. Зекебаев[2], Д.Е. Чен[1], Э.Р. Давлетгильдеев[1]

[1]«С.Ж. Асфендияров атындағы қазақ ұлттық медицина университеті» ҚЕАҚ, Алматы, Қазақстан Республикасы;
[2]«Қазақ онкология және радиология ғылыми зерттеу институты» АҚ, Алматы, Қазақстан Республикасы

COVID-19 пандемия аясындағы сүт безі жергілікті ісігінің сәулелі терапиясының интенсификациясы

Өзектілігі: *Қазақстан Республикасында сүт безі қатерлі ісігі 14,5% үлес салмақпен (2019 жылы – 15,2%) екі жыныс бойынша халық арасында қатерлі ісік ауруларының құрылымында бірінші орынға ие. Бұл жағдай 2004 жылдан бері тұрақты, сонымен қатар, сүт безі қатерлі ісігі әйелдер онкопатологиясы құрылымында бірінші орында және үнемі осы позицияны иеленеді – 44,3‰ (2019 жылы – 51,6‰). 1980 жылдардың басында сүт безі қатерді ісігіне байланысты мамандандырылған көмек көрсету стандарты ретінде сәулелік терапия қолданылды. COVID-19 пандемиясының аясында бізге денсаулық сақтау саласындағы қорларды қайтадан ұйымдастыру үшін басты басымдықтарды анықтау қажеттілігі, сонымен қатар радиациялық әдіс тиімділігінің экономикалық және клиникалық теңгерімі туралы маңызды мәселе туындады. Бұл әдебиет шолу негізгі рандомизирленген сынақтардың нәтижелерін талдауға, сүт безі қатерлі ісігін сәулелік емдеудің гипофракцияланған және стандартты фракциялық режимдерден кейінгі нәтижелерін салыстыруға бағытталған.*

Зерттеу мақсаты: *Негізгі рандомизирленген сынақтардың нәтижелерін талдау және солардың ішінде гипофракциялық (ГФ) және стандартты фракциялық (СФ) режимдеріндегі сәулелік терапияның сүт безі қатерлі ісігін емдеуде нәтижелерін салыстыру.*

Әдістер: *Осы әдебиет шолуда біз сәулелік терапияның гипофракциялық режиміне бағытталған негізгі рандомизирленген зерттеулердің нәтижелерін, қатысқан пациенттердің Американдық терапиялық радиология және онкология қоғамының (ASTRO) әдістемелеріне сәйкес адекватты іріктелуіне мұқият назар аудара отырып, гипофракциялаудың клиникалық практикаға енуіне байланысты оның радиобиологиялық аспектілеріне мән беліп қарастырдық. Зерттеуге қажетті материалдарды іздеу «PubMed» дәлелді медицина дерекқорында 2000-2021 жж аралығында, «радиотерапия», «сүт безі қатерлі ісігі», «дозаны гипофракциялау» кілт сөздерін қолдана отырып жүзеге асырылды. Зерттеуге қосу критерийлеріне T1-3, N0-1 сатыларындағы сүт безі қатерлі ісігі диагнозы қойылған, сәулелік терапияны стандартты фракциялау немесе гипофракциялау режимдерінде өткен, кез келген жастағы пациенттер қатысқан негізгі рандомизирленген зерттеулердің деректері сәйкес келді.*

Нәтижелер: *Негізгі рандомизирленген зерттеулердің нәтижелері бойынша гипофракцияланған режим қалыпты тіндерде болатын кеш әсер бойынша стандартты режимнен ерекшеленбейді және сонымен бірге онкологиялық процесті жақсы бақылауға қол жеткізіледі.*

Қорытынды: *ГФ өзінің тиімділігі мен қауіпсіздігін дәлелдеді, сонымен қатар ерте кезеңдегі сүт безі қатерлі ісігін емдеуде кеш және/немесе жедел сәулелік уытты бойынша одан да жақсы көрсеткіштеге ие және болашақта сүт безін сақтайтын хирургиялық операциядан кейінгі ерте кезеңдердегі сәулелік терапияның жаңа стандарты болуы мүмкін.*

Түйінді сөздер: *радиотерапия, сүт безі ісігі, дозаны гипофракциялау.*

АННОТАЦИЯ

С.А. Копочкина[1], А.Д. Савхатова[2], М.Д. Зекебаев[2], Д.Е. Чен[1], Э.Р. Давлетгильдеев[1]

[1]НАО «Казахский национальный медицинский университет им. С.Д. Асфендиярова», Алматы, Республика Казахстан;
[2]АО «Казахский научно-исследовательский институт онкологии и радиологии», Алматы, Республика Казахстан

Интенсификация лучевой терапии локального рака молочной железы в условиях пандемии COVID-19: Обзор литературы

Актуальность: *Рак молочной железы (РМЖ) в РК занимает первое место в структуре онкозаболеваемости у обоих полов с удельным весом в 14,5% (в 2019 году – 15,2%). Эта ситуация стабильна с 2004 года. Кроме того, РМЖ стоит на первом месте и постоянно занимает эту позицию в структуре женской онкопатологии – 44,3‰ (в 2019 году – 51,6‰). В начале 80-х годов XX века в качестве стандарта оказания специализированной помощи при РМЖ была применена лучевая терапия. Нынешние реалии в условиях пандемии COVID-19 продиктовали нам правила, согласно которым необходимо определить приоритеты для реорганизации средств здравоохранения. Также возник важный вопрос об экономическом и клиническом балансе эффективности способа облучения.*

Цель исследования: *провести анализ результатов ключевых рандомизированных исследований и сравнить результаты лечения РМЖ с использованием различных режимов гипофракционирования и со стандартным режимом фракционирования.*

Методы: *В данном литературном обзоре мы рассмотрели результаты ключевых рандомизированных исследований, посвященных гипофракционированному режиму лучевой терапии, уделив особое внимание адекватному подбору пациентов согласно рекомендациям Американского общества терапевтической радиологии и онкологии (ASTRO) и с учётом радиобиологических аспектов гипофракционирования в связи с его внедрением в клинических условиях. Поиск необходимых для исследования материалов проводился в базе данных доказательной медицины «PubMed» с использованием ключевых слов «радиотерапия», «рак молочной железы», «гипофракционирование дозы», за период 2000-2021 гг. Критериям включения в исследование соответствовали данные крупных рандомизированных исследований с участием пациентов любого возраста с диагностированным РМЖ стадий T1-3, N0-1, прошедших лучевую терапию в стандартном или гипофракционированном режиме.*

Результаты: *По результатам ключевых рандомизированных исследований, гипофракционированный режим не отличается от стандартного режима по поздним эффектам со стороны нормальных тканей и при этом достигается хороший контроль над онкологическим процессом.*

Заключение: *Гипофракционирование доказало свою эффективность и безопасность, а также показывает даже лучшую позднюю и/или острую лучевую токсичность при лечении РМЖ на ранних стадиях и может стать новым стандартом для проведения лучевой терапии на ранних стадиях после органосохраняющей операции.*

Ключевые слова: *радиотерапия, рак молочной железы (РМЖ), гипофракционирование дозы (ГФ).*

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Authors' data:
Kopochkina Sabina Askhatkyzy (correspondent author) – 1-year resident radiation oncologist, Asfendiyarov Kazakh National Medical University NC JSC, address: Almaty city, postal code: 050010, Valikhanov str., 84, apartment #51, e-mail: sabina.kopochkina@gmail.com, ID ORCID: https://orcid.org/0000-0002-0344-6177;
Chen Dmitryi Evgenyevich – 1-year resident radiation oncologist, Asfendiyarov Kazakh National Medical University NC JSC, Almaty city, e-mail: fan.mu.97@gmail.com, ID ORCID: https://orcid.org/0000-0002-7544-3434;
Zekebayev Miras Dyusengalievich – radiation oncologist, Head of day care unit for radiation therapy of Kazakh Institute of Oncology and Radiology JSC, Almaty city, e-mail: zekebaev_miras@mail.ru, ID ORCID: https://orcid.org/0000-0003-2111-5029;
Savhatova Akmaral Dospulovna –Candidate of Medicine, radiation oncologist, Head of day care unit for radiation therapy of Kazakh Institute of Oncology and Radiology JSC, Almaty city, e-mail: akma_s10@mail.ru, ID ORCID: https://orcid.org/0000-0002-3942-480X;
Davletgildeev Eldar Rashidovich – 1-year resident radiation oncologist, Asfendiyarov Kazakh National Medical University NC JSC, Almaty city, e-mail: davl.eldar@gmail.com, ID ORCID: https://orcid.org/0000-0001-8084-936X.