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Review

A review of the international early recommendations for departments organization and cancer management priorities during the global COVID-19 pandemic: applicability in low- and middle-income countries



Yazid Belkacemi ^{a,*,1,2}, Noemie Grellier ^{a,1}, Sahar Ghith ^{a,1},
 Kamel Debbi ^{a,2}, Gabriele Coraggio ^{a,1}, Adda Bounedjar ^{b,1},
 Redouane Samlali ^{c,1}, Pauletta G. Tsoutsou ^{d,1,2}, Mahmut Ozsahin ^{e,1,2},
 Marie-Pierre Chauvet ^{f,1}, Sedat Turkan ^{g,1,2}, Hamouda Boussem ^{h,1},
 Abraham Kuten ^{i,1,2}, Dusanka Tesanovic ^{j,1,2}, Hassan Errihani ^{k,1},
 Farouk Benna ^{l,1}, Kamel Bouzid ^{m,1}, Ahmed Idbaih ^{n,1},
 Karima Mokhtari ^{o,1}, Lazar Popovic ^{p,1}, Jean-Philippe Spano ^{q,1},
 Jean-Pierre Lotz ^{r,1}, Aziz Cherif ^{a,1,2}, Hahn To ^{a,2}, Vladimir Kovcin ^{s,1},
 Oliver Arsovski ^{t,1,2}, Semir Beslija ^{u,1}, Radan Dzodic ^{v,1}, Ivan Markovic ^{v,1},
 Suzana Vasovic ^{w,1}, Liljana Stamatovic ^{w,1}, Davorin Radosavljevic ^{w,1},
 Sinisa Radulovic ^{x,1}, Damir Vrbanc ^{y,1}, Souha Sahraoui ^{z,1,2},
 Nino Vasev ^{aa,1}, Igor Stojkovski ^{aa,1}, Milan Risteski ^{aa,1},
 Salvador Villà Freixa ^{ab,1,2}, Marco Krengli ^{ac,1,2}, Nina Radosevic ^{ad,1},
 Giorgio Mustacchi ^{ae,1}, Mladen Filipovic ^{af,1}, Khaldoun Kerrou ^{ag,1},
 Alphonse G. Taghian ^{ah,1,2}, Vladimir Todorovic ^{ai,1}, Fady Geara ^{aj,1,2},
 Joseph Gligorov ^{r,1}

^a Department of Radiation Oncology and Henri Mondor Breast Center, APHP, INSERM Unit 955 Team 21, University of Paris-Est Creteil (UPEC), France

^b Department of Medical Oncology, Université Blida 1. Laboratoire de Cancérologie, Faculté de Médecine, Blida, Algeria

^c Department of Radiation Oncology, Clinique du Littoral, Casablanca, Morocco

^d Department of Radiation Oncology, Geneva University Hospitals, University of Geneva, Geneva, Switzerland

^e Department of Radiation Oncology, Lausanne University Medical Center and University of Lausanne, Lausanne, Switzerland

^f Department of Surgery, Oscar Lambret Comprehensive Cancer Center, Unicancer, Lille, France

^g Department of Radiation Oncology, University of Cerrahpasa, Istanbul, Turkey

* Corresponding author: CHU Henri Mondor, 51 Av Mal De Lattre de Tassigny, Créteil, 94000, France. Fax: +33 1 49 81 25 89
 E-mail address: yazid.belkacemi@aphp.fr (Y. Belkacemi).

¹ Association of Radiotherapy and Oncology of the Mediterranean area (AROME; www.aromecancer.org). ² TransAtlantic Radiation Oncology Network (TRONE).

- ^h Department of Medical Oncology, University Hospital Abderrahman Mami, Ariana, Tunisia
- ⁱ Department of Radiation Oncology, University of Haifa, Haifa, Israel
- ^j Department of Radiation Oncology, Oncology Institute of Vojvodina, Faculty of Medicine Novi Sad, University of Novi Sad, Serbia
- ^k Department of Medical Oncology, University of Rabat, Rabat, Morocco
- ^l Department of Radiation Oncology, University of Tunis, Tunis, Tunisia
- ^m Department of Medical Oncology, Pierre et Marie Curie, Comprehensive Cancer Center University of Algiers, Algiers, Algeria
- ⁿ Department of Neuro-Oncology, Pitié-Salpêtrière Hospital, Institut Universitaire de Cancérologie AP-HP. Sorbonne University, Paris, France
- ^o Department of Neuropathologie, Pitié-Salpêtrière Hospital, Institut Universitaire de Cancérologie AP-HP. Sorbonne University, Paris, France
- ^p Department of Medical Oncology, University of Novi Sad, Novi Sad, Serbia
- ^q Department of Medical Oncology, Pitié-Salpêtrière Hospital, Institut Universitaire de Cancérologie AP-HP. Sorbonne University, Paris, France
- ^r Department of Medical Oncology, Tenon Hospital, Institut Universitaire de Cancérologie AP-HP. Sorbonne University, Paris, France
- ^s Department of Medical Oncology, Oncomed, Belgrade, Serbia
- ^t Department of Radiation Oncology, International Medical Center AFFIDEA, Banja Luka, Bosnia and Herzegovina
- ^u Department of Medical Oncology, Clinical Center of Sarajevo, University of Sarajevo, Sarajevo, Bosnia and Herzegovina
- ^v Department of Surgery, Oncology and Radiology Institute of Serbia, Belgrade, Serbia
- ^w Department of Medical Oncology, Oncology and Radiology Institute of Serbia, Belgrade, Serbia
- ^x Department of Molecular Oncology, Oncology and Radiology Institute of Serbia, Belgrade, Serbia
- ^y School of Medicine, Juraj Dobrila University of Pula, Radiochirurgia Special Oncology Hospital, Croatia
- ^z Ibn Roshd Anti-cancer Center, University of Casablanca, Morocco
- ^{aa} University Clinic of Radiotherapy and Oncology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, North Macedonia
- ^{ab} Institut Català d'Oncologia, Cap de Servei Oncologia Radioteràpica Hospital Germans Trias i Pujol. Badalona, Barcelona, Spain
- ^{ac} Division of Radiation Oncology, University Hospital "Maggiore della Carità", Novara, Italy
- ^{ad} Department of Pathology and Molecular Pathology, Jean Perrin Comprehensive Cancer Centre, Clermont-Ferrand, France
- ^{ae} Medical Oncology, University of Trieste, Italy
- ^{af} Department of Radiology, Poliklinika Filipovic, Podgorica, Montenegro
- ^{ag} Department of Nuclear Medicine, Tenon Hospital. Sorbonne University, Paris, France
- ^{ah} Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, USA
- ^{ai} Clinic for Oncology and Radiotherapy, Clinical Center of Montenegro and University of Montenegro, Podgorica, Montenegro
- ^{aj} Department of Radiation Oncology, American University of Beirut, Beirut, Lebanon

Received 3 May 2020; accepted 7 May 2020

Available online 8 June 2020

KEYWORDS

Cancer;
 COVID-19;
 Guidelines;
 Recommendations;
 LMICs;
 Health care;
 TRONE;
 AROME

Abstract Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a new virus that has never been identified in humans before. COVID-19 caused at the time of writing of this article, 2.5 million cases of infections in 193 countries with 165,000 deaths, including two-third in Europe. In this context, Oncology Departments of the affected countries had to adapt quickly their health system care and establish new organizations and priorities. Thus, numerous recommendations and therapeutic options have been reported to optimize therapy delivery to patients with chronic disease and cancer.

Obviously, while these cancer care recommendations are immediately applicable in Europe, they may not be applicable in certain emerging and low- and middle-income countries (LMICs). In this review, we aimed to summarize these international guidelines in accordance with cancer types, making a synthesis for daily practice to protect patients, staff and tailor anti-cancer therapy delivery taking into account patients/tumour criteria and tools availability. Thus, we will discuss their applicability in the LMICs with different organizations, limited means and different constraints.

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1. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a new virus that has never been identified in humans before. This virus causes respiratory illness with symptoms like cough, fever and, in most severe cases, pneumonia. At the time of writing of this article, 2.5 million cases of infections have been reported in 193 countries with 165,000 deaths, including Two-third in Europe in accordance with the applied case definitions and testing strategies in the affected countries. This pandemic surprised the whole world by its contagiousness, with a high speed of diffusion in all subpopulations and its violence in terms of deaths.

The Oncology Departments of the affected countries had to adapt quickly and establish new organizations with a practical definition of priorities. Thus, numerous recommendations and therapeutic options have been developed to allow the optimization of departments' organization and function in order to provide and continue to deliver optimal therapy to all patients with cancer.

In these exceptional circumstances, many groups and scientific societies have made practical recommendations. In Europe, the first recommendations concerned mainly the way of protecting patients with cancer [1]. Since then, many guidelines have been proposed for different types of cancers. Obviously, this type of recommendation immediately applicable in Europe may not be applicable in certain emerging countries or low- and middle-income countries (LMICs). Thus, it seemed fundamental to us to summarize these international guidelines according to cancer types and to make a synthesis for daily practice. In addition, we aimed to discuss their applicability in the LMICs with different organizations, limited means and different constraints.

2. Material and methods

To collect the French data, we sent an e-mail to the French Oncology Societies that had not reported guidelines for COVID-19 crisis between March 1st and April 30th. The responses are summarized in Table 1.

For the international literature data, a search in PubMed was performed using the following key words: 'COVID-19 and oncology', 'COVID-19 and cancer', 'COVID-19 and radiotherapy' (RT), 'COVID-19 and guidelines for cancer', 'COVID-19 and recommendations for cancer'. All abstracts and articles in English were collected. Articles in Chinese without English abstracts were not included in the review. In Fig. 1, we summarized the literature search and references that are included in this review. In summary, articles related to oncology guidelines and organization were selected based on the search using the following keywords:

- For 'COVID-19 and oncology': Among the 78 articles, 9 were related to either guidelines/recommendations (n = 5) [1–5] or medical and health system organization (n = 4) [6–9].
- For 'COVID-19 and cancer': Among the 134 articles, 12 were related to either guidelines/recommendations (n = 6) [10–15] or medical and health system organization (n = 6) [16–22].
- For the last 3 key words, namely 'COVID-19 and radiotherapy' (n = 13) [23–29], 'COVID-19 and guidelines for cancer' and 'COVID-19 and recommendations for cancer', the 21 additional references found were redundant and were found with the first two searches (Fig. 1).

All recommendations, including guidelines for RT practice (23–29), have been finally summarized in tables and discussed via e-mails with the AROME and TRONE networks members regarding their applicability in LMICs.

Table 1
Survey from the French oncology societies and clinical research groups.

Type of cancer	Name of the society/group (references)	Response	International scientific societies/Clinical research groups
Head and neck	GORTEC [30,31]	Yes	–
Lung	GOLF [32,33]	–	ESTRO, ASTRO [31]
Breast	Saint Paul-de-Vence [35]	Yes	ASBS [27]
Gynaecological	GINECO	No	Yale University [37]
	SCGP and FRANCOGY [36]	Yes	
GU	GETUG [38]	Yes	–
	CCAFU [12]	Yes	
GI	GERCOR	Yes	ESMO [46,47]
	SNFGE [40]	Yes	
	AP-HP [41]		
Radiation oncology	SFRO [39]	Yes	International radiation therapy network [22]

GI, gastrointestinal; GORTEC, Groupe d'Oncologie Radiothérapie Tête Et Cou; GOLF, Groupe d'Oncologie de Langue Française; ASBS, American Society of Breast Surgeons; SCGP, Société de Chirurgie Gynécologique et Pelvienne; GETUG, Groupe d'Etude des Tumeurs Génito-Urinaires; CCAFU, Comité de Cancérologie de l'Association Française d'Urologie; GERCOR, groupe coopérateur multidisciplinaire en oncologie; SNFGE, société nationale française de gastro-entérologie; APHP, Assistance Publique Hôpitaux de Paris; SFRO, Société Française d'Oncologie Radiothérapie. ESMO, European Society of Medical Oncology.

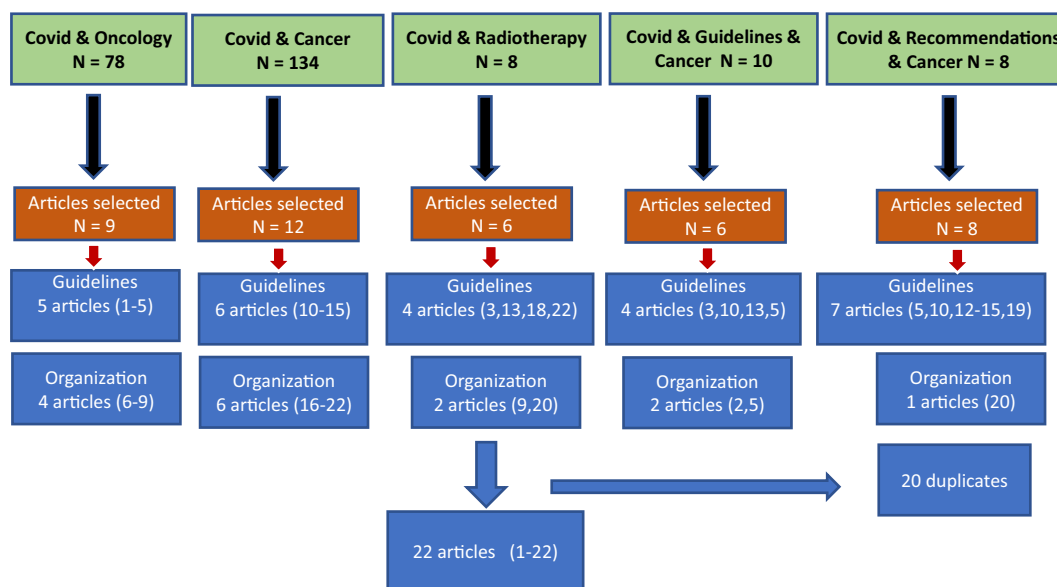


Fig. 1. Results of the literature screening, selection process of articles and keywords.

3. Results

3.1. Patient visits, staff and departments organization (Table 2)

Patients with cancer are more susceptible to infection than individuals without cancer because of the immunosuppressive effect induced by and anti-cancer therapy. In the context of a global public health emergency related to the emergence of COVID-19, it is essential to protect patients and staff to ensure continuity of care. Thus, a major reorganization of our departments was needed to adapt the resources for oncology care maintenance to ensure timely and proportionate implementation of contingency plans that balance risks and protect patients and healthcare workers during the infections rise period. Moreover, the departments reorganization must take into account specifics of the specialities involved in the management of patients with cancer.

3.2. Surgical oncology departments

For surgery, two situations are to be distinguished: patients having undergone surgery just before the COVID-19 outbreak and patients whose surgery is already or must be planned during this period. In the first case, it is reported that COVID-19–positive patients are likely to be at higher risk of clinically severe events than those who did not have surgery. Thus, protective measures must be reinforced and their visits to the department limited. The emergency for adjuvant treatments delivery should be discussed on a case-by-case basis. For scheduled surgery, the discussion will focus on the

delayed interventions, taking into account the benefit/risk ratio for each patient.

In Table 2 some recommendations are presented, from our group (AROME) and others, regarding the prioritization of urgent surgeries and the need to work with the hospital to ensure that adequate supplies (PPE, staffing, and bed capacity) will be available for non-elective, time-sensitive surgeries. Delayed oncologic surgeries may lead to disease progressions and result in tumours that are no longer resectable, leading to worse survival outcomes. Thus, all decisions for delayed surgery ± shift to neoadjuvant therapies should be taken in the frame of multidisciplinary board meetings.

3.3. Radiation oncology departments

In RT departments, staff must also be protected against COVID-19 at all times. Weekly or daily team rotation and dedicated routes for positive COVID-19 patients taken in dedicated time slots with full protection of staff is a prerequisite to reduce the risk to staff and non-infected patients. Tables 2 and 3 show the main reported global and specific recommendations.

In Table 3, we present the main recommendations for workers in RT departments and staff organization, in accordance with available human resources. In addition, scenarios taking into account the reduction in the number of workers in case of COVID-19 infection have been proposed to ensure treatment with the required quality and safety.

For patients, a distinction must be made between patients who have started treatment and those who have not yet started irradiation. For the first, finishing treatment is a priority, either following initial planned fractionation schedules or after plan recalculation to shorten

Table 2

Recommendations for departments organization and procedures for patients, visitors and staff.

Patients and visitors	Patients visits	Staff	Departments organization	Treatments scheduling	References
Minimal presence at hospital	Telemedicine and phone calls		Dedicated areas in oncology and radiotherapy departments	Switch IV treatment to oral drugs when possible	You B <i>et al.</i> [1]
Management at home encouraged			Open space out patients centres	Prioritization according to life expectancy, age, line therapy number	
Separation measures				Temporary breaks for slowly evolving metastases	
Minimise hospital visits and elective Admissions				Consider delaying surgical procedure	Al Shamsi <i>et al.</i> [2].
Consider surveillance for early stage cancer				Consider postponing adjuvant CT and RT but hold any active therapy	
				For all patients on active anti-cancer therapy remain vigilant for COVID-19 symptoms	
To manage currently infected patients Schedule outpatients based on priority criteria	In-house isolation or quarantine of suspected cases to keep hospital admissions manageable	N95 mask fitting	Clear delineation of job responsibilities	Integrate all best-practice approaches into work processes to prevent further transmission	
Isolate patients with suspected infection until they are cleared		Prompt identification of suspected infection among staff and application of appropriate isolation			
Patients and visitors screening before appointments	Limitation of visitors in departments	Staff temperature screening every day Staff rotation schedules	Separate Entrance/exit	Maintain therapy schedule according to the benefit risk and availability of means for locally advanced and high-risk, patients and those already started their therapy.	Applicability in LMICs
Specific plan for COVID-19 suspected or positive	Should be limited	Staff COVID-19 + out of planning and self isolation 14 days	Space with limited patients in waiting room	Deep remission (3–6 months) stopping therapy is an option	
Separate cancer patients from other patients			Treatment of COVID-19+ patients outside of cancer center or dedicated area		

COVID-19, coronavirus disease 2019.

treatment duration. For the weekly visits, telemedicine and phone calls could be advocated to limit the time spent in the hospital every day. For COVID-19–positive patients, dedicated areas, separate exit/entrance and dedicated time slots have to be planned.

For patients who have not started RT yet, priorities should be also fixed as per tumour sites, adjuvant or neoadjuvant settings, the possibility of delaying irradiation in settings where primary chemotherapy or endocrine therapy could be administrated. These situations will be discussed in the next section.

3.4. Medical oncology departments

As for other departments, dedicated areas, specific exits/entrance and a limited number of patients in the waiting rooms are recommended to limit contacts between infected and non-infected patients. To ensure minimal presence in the hospital, some regimens can be altered to minimize infusion visits or a switch to oral drugs when possible. During treatments, systematic screening before appointments is recommended by the majority of experts.

Table 3
Radiation Oncology departments organization during COVID-19 pandemic period.
Recommendations for radiotherapy departments organization

Societies/groups/teams	Frenche RO society [39]	Simcock <i>et al.</i> [22]	Applicability in LMICs
	March 19th	March 20 th	
Workers protection			
WHO guidelines for preventive measures and use of Personal Protection Equipment (PPE)	X	X	Applicable
Reduction of the number of health professionals in radiotherapy departments to the minimum required, promoting teleworking	X	X	Teleworking probably not
Inviting the local Infection Control department		X	
Temperature monitoring for all patients		X	Applicable
Special monitoring for 'contact' patients (those who had close contact with confirmed COVID cases)	X		Probably not
Symptomatic health professional: PCR, isolation, adapted care	X		Probably not
Department Organization			
Delay of follow-up medical examinations	X		Applicable
Remote/telephone consultation when possible	X	X	Probably not
Minimize number of additional visitors, family members or careers		X	Applicable
Reorganization of waiting rooms (separating fragile vs potentially infected patients, increased distances, removal of infection vectors)	X	X	
Optimize department areas for decontamination		X	
Model for estimation of the harms of COVID infection for cancer patients		X	
Creating capacity by reducing fraction numbers		X	
Separation of fragile/immunocompromised vs infected/contact patients	X		
Special protocol for infected/contact patients (treatment pause or dedicated treatment timeslot)	X	X	
When Insufficient Number Of Health Professionals			
Priority to: primary radiation treatments (vs operable or adjuvant), curative (vs palliative)	X	X	Applicable
Delay treatment for hormone-sensitive cancers ^a		X	
Record all changes in treatments	X		
Only one therapist per treatment (standard)	X		
Two therapist per treatment (complex treatments)	X		
Turnover for radiation oncologists and medical physicist	X		
Brachytherapy			
Delay of all brachytherapy treatments		X	Applicable
Prefer local/spine anaesthesia to general anaesthesia	X		
Delay of treatments where surveillance is an alternative option	X		
Priority to: primary treatments (vs adjuvant), single treatment (vs fractionated)	X		
FFP2 masks for head and neck treatments	X		
Special cases dealt with			
Insufficient number of medical physicists	X		Applicable
Insufficient number of radiation oncologists	X		
Increase of quality control hours and prioritization of checks	X		
Specific indications for omitting/delaying/hypofractionating/pausing radiotherapy treatment by cancer type and curative vs palliative treatment		X	

COVID-19, coronavirus disease 2019; LMICs, low- and middle-income countries.

^a With attention on a post-crisis unmanageable surge in activity. RO: radiation oncology.

For patients already in deep remission (stable for more than 6–12 months), stopping or delaying treatment may be an option. A temporary break could be an option for patients with slowly evolving metastases. For all patients on active anti-cancer therapy, we need to remain vigilant for COVID-19 symptoms. Their therapy should be planned in a dedicated area.

Changes in management strategy and therapy in accordance with type of cancer (Table 4).

3.4.1. Head and neck cancer

The medical complexity of head and neck cancer management may lead to prolonged delays that worsen treatment outcomes. Therefore, those caring for patients with head and neck cancer must take action to reduce these negative impacts as the country rallies to overcome the challenges posed by this pandemic [24]. Thus, therapeutic adaptation possibilities reported by the French groups are based mainly on expert opinion [30,31].

Table 4

Approach to curative intent therapy by tumour sites: summary of the published recommendations during COVID-19 crisis.

Disease	Criteria for delay	Fractionation	Boost	Systemic therapy	References	LMIC applicability
Head and neck						
Head and neck cancer: all tumour sites	Head and neck cancer treatment break or deferral may lead to reduced tumour control Patients < 70 y, with non resectable tumours: Standard time for treatment ≤ 4 weeks since diagnosis should be respected Patients <70 y, eligible for adjuvant RT: A period of 6–8 weeks between surgery and RT should be respected. Patients >70 years old or unfit (≥PS 2 and/or with significant comorbidities) HPV	Consider mitigating with additional radiation dose after treatment or addition of chemotherapy. SIB should be considered: -69,96Gy/54.45 in 33 fractions -69Gy/55 in 30 fractions Consider published hypofractionated schemes: 50–52.5 Gy in 16 fractions for larynx T1N0 -R1 and/or extra-capsular rupture: 66 Gy/54 Gy in conventional fractionation, -otherwise 60 Gy or 50 Gy depending on the histo-prognostic factors Non resectable tumours: -30 Gy in 10 fractions -10–12 days later: 25 Gy in 10 fractions or 24 Gy in 8 fractions Adjuvant: -SIB: 51Gy/42.5 in 17 fractions or any other hypofractionated schedules no de-escalation for HPV + tumours		Concomitant chemotherapy for locally advanced forms should be offered according to the usual indications Concomitant chemotherapy for high risk tumours should be offered according to the usual indications	[30,31]	Applicable Applicable only if IMRT is available. Beside small volumes (such as larynx T1 N0), hypofractionation using 3D RT = risk of high toxicity To favour chemotherapy during the first 2 months before combined chemoradiation Applicable for palliative care Not applicable
Lung cancer Early NSCLC	No delay of post-op RT No immediate RT for N2 NSCLC	Standard RT		Standard therapy –3 cycles of CT - Carboplatin is preferred over cisplatin - Systematic administration of GCSF	[32,33]	Applicable
Locally advanced NSCLC	No delay of CRT	Standard RT	Standard therapy - Carboplatin is preferred over cisplatin - DURVALUMAB: double dose/4 weeks			Not applicable
Metastatic NSCLC	PS 1, Fit patients PS 2, elderly patients	Palliative strategy	Oncogenic alteration: standard therapy No oncogenic alteration: – 4 cycles of CT/Immunotherapy - Maintenance CT: spacing or arrest -Pembrolizumab:			According to availability of immunotherapy Applicable

SCLC	No delay of CRT	Standard RT	Arrest of treatment for responding patients or double dose/6 weeks for non-responding.	-Standard therapy -Carboplatin is preferred over cisplatin -Systematic administration of G-CSF		Applicable If G-CSF available
Breast DCIS	Delete RT 3–6 months	40Gy in 15f			TAM “standby” therapy possible	[3,35] Applicable
Invasive BC HR + post M stages I II	Delete RT 3–6 months	Preferred scheme 40Gy in 15f	Not systematic boost in low risk		ET standby therapy systematic	
Other BC subtypes and patients profiles including young and high- risk patients	No delay of RT	Standard or hypofractionation	Hypofractionation boost: 10–15Gy OR Integrated boost		Standard therapy	
GU – Prostate Low risk	Active surveillance or delay treatment	–			–	[12,38] Applicable
Intermediate risk	Delay RT 3 months	In case of RT indication use hypofractionation (60Gy in 20fr)			3–6 months of ADT before RT	[39] Hypofractionation only if IMRT is available and no indication of nodal RT
High risk	Delay surgery by 3–6 months Delay RT by 3–6 months Surgery should be switched to RT				No ADT 3–6 months of ADT before RT	[12, 39] Applicable Using standard fractionation No dose escalation if IMRT-IGRT no available
Post-operative or “rising PSA” RT indication Metastatic setting hormone sensitive Castration-resistant patients	Delay RT by 3 months Delay RT for oligo-metastatic disease Delay/avoid CT and prednisone				3 months of ADT before RT ADT + New generation of ET Enzalutamide is to be preferred	[12] If Enzalutamide is available
GU – Bladder Muscle infiltrating (MI)	Surgery, no delay				NA Chemotherapy possible	[38] Applicable
MI when surgery is contraindicated	RT with or without 5Fu/myto	In case of RT indication hypofractionation should				[38, 39] Hypofractionation only if IMRT is available a (continued on next page)

Table 4 (continued)

Disease	Criteria for delay	Fractionation	Boost	Systemic therapy	References	LMIC applicability
Metastatic 1st line	cisplatin-gemcitabine + G-CSF (No MVAC)				[38]	Applicable If G-CSF is available
Metastatic 2nd line	Delay treatment		Unknown impact of checkpoint inhibitors on covid19			–
GI – oesophagus						
Localized cancer	RTCT with Carboplatin-Taxol	Standard			[40–47]	Applicable
Inoperable or advanced	Standard		Or FOLFOX			
Complete response to CRT	Follow-up or delay surgery					
Incomplete response to CRT	Delay salvage surgery up to 3 months					
GI-Pancreas						
Operable/bordrline	Patients who does not fit for neo-adjuvant chemotherapy should be considered as high priority for surgery			NA FOLFOX to delay surgery	[40, 47]	Applicable according to drugs availability
Locally advanced	Avoid CRT during COVID-19 outbreak Completion of NA chemotherapy when already started or patients included in clinical trials should be also considered as a high priority			CT with schemes using Capecitabine		
Post-operative setting	Delay adjuvant treatments according to the benefit risk			FOLFIRINOX is recommended (depending on benefit in OS)	[40]	
GI – Rectum						
CRT completed or ongoing	Delay surgery up to 3 months				[40, 42–44]	Applicable
All new patients	Pre operative RT	25Gy in 5fr and surgery after 3 months				
T4 rectal cancer	Chemoradiation	CAP 50 and surgery after 11weeks				
Low rectum with complete response to chemoradiation	Tumour excision or watch and wait (GRECCAR 2 criteria)					
GI – Anal canal						
Localized	Standard chemo-radiation based on capecitabine or mytomicin C				[40, 47]	Applicable
Recurrence or metastatic setting	Chemotherapy with capecitabine/oxaliplatin or carboplatin/capecitabine					

Gynaecological – Cervical cancers

Cervical cancer	-No delay of RT or RCT -Delay of LN staging surgery -No RT in the in case of complete response	Standard RT or RCT	[36, 37]	Applicable
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Gynaecological – Endometrium

Low and intermediate risk or stage IA	Delay surgery up to 1–2 months	Total hysterectomy with bilateral annexectomy associated with sentinel node procedure		Applicable
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High-risk or stage II	- To favour the MSKCC algorithm (PET CT + sentinel node procedure) in order to omit LN dissection - Delay of RT according to the benefit/	Consider if brachytherapy alone is a reasonable substitute for these patients after weighing risks and benefits		PET-CT availability
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Advanced stage III IV	- Primary chemotherapy - Delay RT	6 cycles of Carboplatin - Taxol up-front and then delay the pelvic RT until after chemotherapy completion.		Applicable
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Gynaecological – others

Vulvar cancer	Early-stage: surgery could be delayed up to 1–2 months No surgery indication: RTCT without delay			Applicable
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Vaginal cancer	To favour imaging for staging in order to omit LN surgery RTCT if no surgery indication without delay			
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Ovarian	Early-stage: delay surgery up to 1–2 months Advanced stage: to favour primary systemic therapy No intraperitoneal hyperthermia chemotherapy (CHIP).			Not available mainly
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RTCT, radiochemotherapy RT, radiotherapy; NA, neoadjuvant; LN, lymph nodes; COVID-19, coronavirus disease 2019; LMICs, low- and middle-income countries; MSKCC: Memorial Sloan Kettering Cancer Center; PET-CT: positron emission tomography-computes tomography; G-CSF: Granulocyte colony-stimulating factor

Thus, in daily practice, any adaptation must be discussed with the patient and in the frame of multidisciplinary board meetings. For surgery community, the aim is to minimize the risk of care opportunity loss for patients and to anticipate the increased number of cancer patients to be treated at the end of the pandemic, taking into account the degree of urgency, the difficulty of the surgery, the risk of contaminating the caregivers (tracheotomy) and the local situation (whether or not the hospital and intensive care departments are over-stretched) [30,31].

All indications for combined chemoradiotherapy must be maintained, as well as the usual delays between diagnosis and RT (≤ 4 weeks) or between surgery and RT (6–8 weeks). Fractionation must be optimized: favour hypofractionation (early-stage larynx, elderly or comorbid patients) and simultaneous integrated boost [30].

3.4.2. Lung cancer

Following the ESTRO (European society of therapeutic radiation oncology)-ASTRO (American society of therapeutic radiation oncology) consensus statement [32] and the French recommendations [33], we need to distinguish recommendations according to pathology and stage of the disease.

For early non-small-cell lung cancer, surgery could be delayed up to 6 weeks for stage I II, N0 disease. Another alternative approach is to deliver stereotactic RT with a limited number of fractions (1 to 3).

In the post-operative setting, patients undergoing treatment have to complete their program. For adjuvant RT, given the uncertainty about its impact in this context, it is not recommended to initiate RT for patients with N2 disease.

In locally advanced non-small-cell lung cancer, patients are more at risk of developing severe respiratory acute complications requiring intensive care. Thus, only patients who are already undergoing therapy should complete their program while initiation of RT in new patients is discussed in the frame of multidisciplinary board meetings. For patients undergoing chemotherapy, carboplatin is preferred over cisplatin for its rapidity of administration and its lower toxicity.

The administration of durvalumab must be carried out if the safety conditions are reasonable, by adapting the treatment regimen [33].

3.4.3. Breast cancer

The American Society of Breast Surgeons (ASBS) [34], the French Saint Paul-de-Vence (SPDV) group [35] and the international RT network [3] reported their recommendations in March. The ASBS recommended breaking into three priority categories based on patient conditions, ranging from immediately life-threatening conditions to patients stable enough that services can be delayed for the duration of the COVID-19 pandemic.

In the SPDV conception, different scenarios were detailed.

In summary, for post-operative patients and those on follow-up telemedicine is recommended. Interventions for biopsies in abnormal mammograms, neoadjuvant patients finishing treatment, hormone therapy during 6–12 months for luminal hormone receptor (HR)-positive patients, adjuvant antibody treatment reasonably be curtailed after 7 months instead of 12 months of treatment for HER2-positive and limit reconstructive surgery to expander only are the main recommendations. In addition, more specifically in patients with breast luminal cancer (early or locally advanced) primary endocrine treatment could safely delay surgery up to 3 to 6 months, in a accordance with several published trials.

For adjuvant RT, up to 16 weeks of last surgery or chemotherapy with high-risk indications for radiation, such as inflammatory disease, node positive disease, triple negative breast cancer, post-neoadjuvant chemotherapy with residual disease at surgery, young age (< 40) with additional high-risk features, are recommended.

Patients older than 65–70 y with lower risk stage I HR-positive/HER2- negative cancers and ductal carcinoma in situ (DCIS), adjuvant endocrine therapy can be encouraged to defer/omit radiation without affecting overall survival. Hypofractionated regimens are recommended, including in cases of DCIS, post-mastectomy or nodal RT. The boost is reserved for high-risk patients, and SIB or hypofractionation is to be preferred [3,22,29,35].

3.4.4. Gynaecological cancers

Since the beginning of March, numerous scientific societies and research groups provided recommendations for cervical, endometrial and ovarian cancer [36,37].

In summary, for cervical cancer, it has been suggested that the value of lymph node staging surgeries must be reviewed on a case-by-case basis in accordance with comorbidities, imaging results and stage of disease. For therapy, the recommendation is to omit any changes in radiochemotherapy regimens or interrupt or postpone RT that could lead to tumour response reduction. After concomitant radiochemotherapy, surgery should not be systematic in cases of complete response.

In endometrial cancer, recommendations are in accordance with the stage of disease [36]. Surgery remains the standard of care for early-stage disease. The minimally invasive laparoscopic approach, robot-assisted (or not) is the preferred approach. For low and intermediate pre-operative European society of medical oncology (ESMO) risk, total hysterectomy with bilateral ovariectomy associated with a sentinel node procedure should be preferred. It is lawful to consider postponing surgery by 1–2 months in low-risk endometrial cancers. For high ESMO risks involving staging

by pelvic and lumbo-aortic nodal dissection, it seems recommended to favour the Memorial Sloan Kettering Cancer Center (MSKCC) algorithm, associating positrons emission tomography - computed tomography (PET-CT) and sentinel node biopsy procedure to omit nodal dissection which increases the risk of pre- and post-operative complications.

For ovarian cancers, recommendations are as per the stage of disease. For early-stage ovarian cancer, surgery may be postponed by 1–2 months, whereas for advanced disease, neoadjuvant chemotherapy or primary ‘debulking’ surgery should be considered. In cases of neoadjuvant chemotherapy, additional cycles up to 6 could be considered before surgery [36].

For vulvo-vaginal cancers, the main messages consist of delaying surgery by 1–2 months and indicate chemoradiation in locally advanced cases, whereas PET-CT for staging should be favoured to delay lymph node dissection.

3.4.5. Genito-urinary cancers

Recommendations concerned mainly prostate, bladder and kidney cancers. In summary, the French recommendations [12,38] for prostate cancer are oriented towards delaying all RT planning by 3–6 months. During this period, ADT administration is recommended in intermediate and high-risk patients. For RT, schedules should be hypofractionated if RT is started during the COVID-19 period [39,40]. For low-risk patients, surgery could be delayed in favour of active surveillance. Moreover, surgery should not be delayed more than two months in high-risk and locally advanced patients [12]. This will be considered in accordance with the availability of operating rooms and the post-operative complications risk.

In patients with bladder cancer, surgery should not be delayed more than three months in the majority of cases. When RT is indicated, it should be hypofractionated. Primary chemotherapy and number of cycles should be discussed on a case-by-case basis. If surgery is preferred, a maximum of three months after diagnosis is proposed [12].

For the kidneys, beside locally advanced and thrombosis situations, surgery has to be delayed after confirmation in the tumour board [12].

3.4.6. Gastrointestinal cancer

In summary, surgery could be postponed by three months for gastrointestinal (GI) cancers when other therapies are indicated. All decisions should be taken in accordance with the stage of the disease and the risk of spread in case of delaying optimal therapy [25].

Oesophagus cancer should be treated whenever possible with RT and concomitant carboplatin and taxol. In the neoadjuvant setting or salvage therapy, surgery could be delayed up to three months [40,41]. Detailed RT recommendations, including definitive

combined radiochemotherapy and fractionation have been reported by Jones et al. [26]. They also suggested that as the impact of RT on disease severity in patients with a diagnosis of COVID-19 is unknown and it may be appropriate to avoid RT in such patients.

Surgery for rectal cancer should be delayed up to three months [40] and neoadjuvant treatment for new patients should be carried out with the short-course scheme [40,42], reserving the classical CAP50 therapy. The watch and wait attitude is possible for patients with complete response after standard chemo-RT [40,43,44]. In anal canal carcinomas, chemo-RT capecitabine should replace 5-FU+/- mitomycin C[40,45]. Brachytherapy, if indicated, could be delayed [39].

For pancreatic and other GI cancers, ESMO guidelines defined high priorities for surgery and systemic therapy [46,47]. All resectable cancers and borderline patients who are not fit for neoadjuvant chemotherapy should be considered as high priority. In locally advanced disease, initiation or completion of neoadjuvant chemotherapy when already started or patients included in clinical trials should be also considered as a high priority [47].

4. Discussion

This review aims to summarize some national/international guidelines and literature regarding the organization of patient management and specific recommendations by tumour sites. Indeed, outbreaks of COVID-19 disease may result in the interruption of medical care provided to patients with cancer and induce undertreatment in addition to the risk of infection and death from COVID-19. Early data from China and Italy suggest that patients with cancer may be at higher risk of contracting COVID-19, particularly when multiple visits are needed, and also developing more severe forms of the disease [48,49]. One prospective study on 1590 patients pointed out the higher incidence of COVID-19 in patients with cancer [49]. In addition, patients with cancer seem to be at a greater risk of ventilation need and death [50,51]. Thus, preventing patients with cancer from being exposed to COVID-19 is a critical public health priority that needs an important effort in terms of staff and department organization and patient screening to adapt therapy delay and management despite COVID-19 infection risk. The benefit risk/ratio is a key point for all newly diagnosed cancers, as delaying treatment is not recommended if, at all, avoidable [28,52].

In LMICs the problem of delay in diagnosis already exists. So the fear with the COVID-19 pandemic is to see an increase in the number of patients with locally advanced cancers who do not receive treatment in time. In certain countries, with the screening program being stopped during the pandemic, locally advanced forms

may resurface in local epidemiology if screening remains suspended for a long time. For head and neck cancers for example, a panel from ASTRO and ESTRO have published statement with two pandemic scenarios: early (risk mitigation) and late (severely reduced RT resources) and treatment recommendations for five head and neck cases. There was agreement (or strong agreement) across a number of practice areas including: treatment prioritization, whether to delay initiation or interrupt RT [27].

In the last three months, a number of scientific societies, oncology groups and experts' networks have suggested that all efforts should be made to prevent patients with cancer from being exposed to COVID-19. They also proposed several recommendations for urgent new organization in oncology departments with possible patient selection, treatments and schedules tailored in accordance with patients and tumour criteria, so as to continue to provide adequate strategy for the majority of patients [1,2,7,11,16].

In accordance with the local health system organization and tools availability, different approaches have been undertaken by cancer centres and oncologists in countries with early epidemics, in response to the risk of infection, as well as strain on health systems. The main proposals are summarized in [Tables 2 and 3](#). They are as follows:

- (i) Minimizing the risk of exposure for patients (with a clear policy of screening before appointments) and staff (with daily temperature screening) to protect the immune compromised patients.
- (ii) Department reorganization with minimizing patient turnover times ('fast track' area) and number of visits to the hospital. Use of telemedicine and phone calls for postponed appointments and non-urgent surgeries or other treatments [53,54].
- (iii) Delaying locoregional therapy data to reduce risk of COVID-19 in patients with cancer are limited. The American College of Surgeons recommends balancing the risk of delay of an elective surgery with the potential likelihood for a post-operative need for respirator utilization [54]. In addition, patients with a history of surgical resection may have continued immunosuppression or other prolonged effects of surgery, which can contribute to COVID-19 risk [55].
- (iv) Shortening RT duration and plan recalculations for hypofractionated schedules have been proposed in accordance with the type of cancer and curative or palliative intent situations. In some cases (e.g., low-risk breast and prostate cancers), endocrine therapy is advocated to delay RT by 2–4 months [3,38,39].
- (v) Switching patients from intravenous to oral therapies to limit the number of inpatient visits has been recommended in France [1] and Italy [52]. In all cases, delaying systemic therapy is not recommended if at all avoidable [52]. For patients already in deep remission (stable for more than 6–12 months), stopping treatment may be an option [1,2,35].

The vast majority of the published recommendations for department organization, staff and patients' appointments/visits are quite feasible in the majority of LMICS. At times, there may be complex geographic situations, unavailability of equipment or means of communication (telemedicine) and staff which can negatively impact the situation. The selection of patients for whom care can be deferred becomes a major issue in the organizational management of the weeks in which the contagiousness to COVID-19 is high. However, the definition of priorities can be complicated to do in certain LMICs. For example, the NICE recommendation says that during COVID-19 pandemic 'use RT only if unavoidable' [28]. This could be in agreement with the availability of resources and means in LMICs unlike others [28–32] are more precise in terms of patients' selection that takes into account cancer type and disease stage to not compromise the prognosis.

[Table 4](#) summarizes the main recommendations by tumour sites. There is mainly a deal between avoiding COVID-19 contamination for patients without making them lose chances of cure due to deferring or suspending standard effective treatment. Even if limited evidence exists on the modification of treatment plans to reduce the risk of COVID-19 in patients with cancer, these recommendations are an important support for many oncologists to help with the decision. Adapted to the local situation, they can also serve as a basis for decisions in LMICs. However, we must note the fact that, in addition to the limited means in some countries, the local epidemiological context can limit these recommendations applicability. One example is combined radio chemotherapy for oesophageal cancers. In case of unavailable modern techniques in these countries that could avoid significantly organ at risk exposure, ovoiding RT has been suggested as an option as the disease severity expected in patients with a diagnosis of COVID-19 is unknown [26].

For surgery scheduling, the American College of Surgeons recommends balancing the risk of delay of an elective surgery with the potential likelihood for post-operative ICU or respirator use [54]. Presumably, in certain LMICs, oncological surgery continues to be carried out in general surgery departments which are very widely transformed into UCI during the COVID-19 crisis. Thus, this transformation necessary to take care of patients with COVID-19 with respiratory distress directly impacts the cancellation of oncological surgery.

Whatever the type of cancer, the consensus is to postpone surgery. The most obvious cases concern those who benefit from screening, such as breast and prostate cancer. The recommended delay can go up to 2–3 months. However, patients' selection for delaying surgery is a crucial point, as delayed oncologic surgeries may lead to disease progression and result in tumours that are no longer resectable, leading to worse survival

outcomes [52]. For locally advanced and high-risk patients, neoadjuvant therapies represent a solution before undergoing surgery in breast and some GI cancers [12,38]. The dilemma in this case is to weigh the risk/benefit ratio of treating patients optimally during the COVID-19 period with the consequences of immunosuppression [55,56] and repeated visits to the hospital to receive RT when it is indicated for combined therapy. The delay between the end of pre-operative treatment and surgery can also be lengthened in many cases, such as rectal [43], endometrial [36] and bladder cancer [12,38].

In addition, prior RT, the primary treatment, can constitute a “waiting” solution during the COVID-19 period. The recommendations are fairly unanimous for high-risk and locally advanced prostate cancers [12,38,39]. Indeed, as the radiohormonotherapy trials of prostate cancer have all used schemes with a primary hormone therapy between 2 and 6 months before RT, it is easier to defer the RT (up to 6 months) without any prejudice for the patient [38,39]. Recently, Zaorsky *et al.* [23] have to establish recommendations and a framework by which to evaluate prostate RT management decisions. They concluded that the Remote visits, and Avoidance, Deferment, and Shortening of RT framework can be applied to prostate cancers and other disease sites to help with decision-making in the COVID-19 pandemic. This concept could be applicable in LMICs with however some specificities regarding local situations of health care and means.

For breast cancer, the data are less robust for primary endocrine therapy while ‘waiting’ for RT. However, the consensus recommends in many situations to postpone or even omit RT in elderly patients with low risk, as no evidence of impact on survival has been demonstrated in this subset of patients [35].

RT hypofractionation, already largely used in LMICs, is systematically recommended in the adjuvant setting without chemotherapy. A recent report from USA has pointed out the evidence-based guidelines for omitting or abbreviating breast cancer RT, where appropriate, in an effort to mitigate risk to patients and optimize resource use [29].

In breast and prostate cancer, high evidence of equivalence between standard and hypofractionation has been demonstrated in the literature. However, in prostate and breast cancer, this is generally true only for limited irradiation volume in patients without extended nodal RT. Large volume of lung RT could increase the risk of lung damage if the patient became infected by COVID-19 during RT and developed severe respiratory acute syndrome [57].

For systemic therapies, there is currently no evidence to support changing chemotherapy and immunotherapy regimens. In addition, delaying treatment is not recommended if at all avoidable [52]. However, some regimens can be altered to minimize infusion visits. For all

cytotoxic regimens, dose intensity is important and multiple studies report poorer survival in cases of dose intensity reduction. In the surgical consensus, the option of an increased number of cycles allowing a surgery delay of 2–6 weeks is advocated [12,33]. However, this should be carried out with caution regarding treatment efficacy and its potential toxicity. In cases of systemic therapy maintenance, switching IV to oral therapies largely available in LMICs, is mostly recommended to limit the number in-patient visits to the hospital. For patients already in complete remission, stopping or delaying treatment may be an option. The use of systemic treatments is not contraindicated during the COVID-19 pandemic period. However, given the risk of possible immunosuppression, it is important to discuss the indications and to prioritize the treatment strategies in accordance with the benefit-risk ratio as this has been underlined in the various reference systems cited previously [46,47,52].

5. Conclusion

The COVID-19 pandemic has and will have a major impact on the organization of healthcare systems. While novel vaccines and drugs that target SARS-CoV-2 are under development, the challenge for oncology community is to continue to provide the best therapy to all patients. It will be crucial to consider the benefit risk ratio for optimal anti-cancer therapy (to minimize the risk of care opportunity loss for patients) and minimize COVID-19 contaminations during therapy that may interrupt or delay therapy, and thus, compromise patients’ outcome. Several recommendations published from the early period of the crisis have helped for urgent new organization in oncology departments with possible patient selection, treatments and schedules tailored according to patients and tumour criteria.

In LMICs, the challenge is to define strategies to try mitigating the deleterious effect of COVID-19 pandemic on cancer care. These negative effects will be probably amplified due to (i) epidemiology of cancer diagnosed in more advanced stages in these countries, (ii) limited means for diagnostic and treatment that will delay cancers management; (iii) the need to manage COVID-19 patients in limited number of centres that will impose delay for cancer therapy and (iv) the economic impact of the COVID-19 pandemic on health system priorities and investment in oncology.

Of note, the vast majority of these recommendations for department organization, are quite feasible in the majority of LMICs where the context for cancers patients is related multiple parameters such as: late diagnosis, long waiting lists for therapy and the lack of therapeutic innovations due to the economic situation which may be worsened by the COVID-19 pandemic.

Financial support

None.

Conflict of interest statement

A.I. declares the following relevant financial activities outside the submitted work: has received Grants from Transgene, Sanofi, Air Liquide, Nutritheragene; has received travel funding from Leo Pharma; Grant research support and travel funding from Carthera. J.G. declare the following financial personal fees for activities outside the submitted work or served as consultant or advisory board/ has received symposium and travel funding from: Roche-Genentech, Novartis, Onxeo, Dachii Sankyo, MSD, Isai, Genomic Health, Ipsen, Macrogenics, Pfizer, Mylan, Lilly, Immunomedics, Sandoz. J.-P.S. declares the following financial personal fees for activities outside the submitted work or served as consultant or advisory board/ has received Symposium and travel funding from: MSD, Lilly, Roche, Mylan, Pfizer, PF Oncology, LeoPharma, Novartis, Biogaran, Astra Zeneca, Gilead, BMS. All the other authors have no conflict of interest to declare.

Acknowledgements

The authors would like to thank Ms Myrna Perlmutter for her help in editing English language for this manuscript.

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