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Original Article

Oncology Section

Dosimetric and Volumetric Analysis in Endobronchial Brachytherapy in Lung Carcinoma: A Cross-sectional Study

RAVI KANT[1], MEENU GUPTA[2], JYOTI BISHT[3], VIPUL NAUTIYAL[4], VINEY KUMAR[5], RISHABH DOBHAL[6], MUSHTAQ AHMAD[7], SUNIL SAINI[8]

ABSTRACT

Introduction: High Dose Rate (HDR) brachytherapy plays an important role in the treatment of lung carcinoma. The treatment of lung carcinoma with Endobronchial Brachytherapy Treatment (EBBT) is delivered in three fractions and the effect of EBBT on the Target Volume (TV) after delivering the three fractions in the lung carcinoma needs to be assessed. The TV is covered with the prescribed dose and Organs At Risk (OARs) doses are evaluated.

Aim: To assess the doses to OAR nearby the tumour and analyse the effect of the TV, tumour location, and site on the doses to OARs in EBBT in lung carcinoma.

Materials and Methods: A cross-sectional study was conducted in the Department of Radiation Oncology, Cancer Research Institute, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University Dehradun, Uttarakhand, India, from January 2018 to December 2020. Thirty patients with lung carcinoma were included in dosimetric and volumetric assessments. A flexible lumencare catheter was inserted into the bronchial lesion. Computed Tomography (CT) scan was acquired and exported to Treatment Planning System (TPS) through Digital Imaging and Communications in Medicine (DICOM) networking system. An optimised treatment plan was generated. The TV and OARs were delineated on the CT scan of the patient. A total of three EBBT sessions were given with a 7 Gy dose per fraction and prescribed the dose at 1.0 cm from the center of the catheter. Doses to OARs and the effects of TV on doses to OARs were evaluated with the help of "Dose Volume Histogram (DVH) tool" in the TPS. Thirty patients, with varying TV and site, were grouped as left lung and right lung tumour lesions and also grouped as TV <22 cc and TV >22 cc for the analysis purpose in this study. The data was entered in Microsoft Office Excel 2007 and analysed in Statistical Package for the Social Sciences (SPSS) version 22.0 statistical analysis software (IBM Corp., Armonk, N.Y., USA) tool.

Results: The mean doses to OARs in 1st, 2nd and 3rd EBBT sessions were within their tolerance limit. The mean dose difference between left and right lung tumour site were analysed and found mainly the mean dose to oesophagus and maximum dose to oesophagus, contralateral lung, left coronary artery and descending aorta were significantly higher in left lung compared to right lung with p-value 0.015, 0.027, 0.001, 0.007 and 0.001, respectively. The maximum dose to the contralateral lung and spinal cord were significantly higher in middle-lower bronchial lesion with p-value 0.024 and 0.023, respectively. The mean dose difference between left and right lung tumour volume for TV <22 cc and TV >22 cc was analysed and found mainly for the group TV >22 cc the mean dose to oesophagus and maximum dose to oesophagus, Heart, contralateral lung, left coronary artery and descending aorta were significantly higher in the left lung compared to right lung with p-value 0.002, 0.008, 0.027, 0.003, 0.006 and 0.001, respectively whereas in the TV <22 cc group only the contralateral lung max dose was significantly higher in left lung compared to right lung with p-value 0.046.

Conclusion: The OARs doses were increased significantly in left lung compared to right lung carcinoma. The TV was large in the middle-lower bronchial region, therefore, the doses were found higher, and TV in the lower bronchial region is less so the dose was less.

Keywords: Bronchial lesion, Dose volume histogram, Fraction, Organ at risk, Target volume

INTRODUCTION

The HDR brachytherapy plays an important role in the treatment of lung carcinoma. A radioactive source Ir-192 provides a very high dose to the tumour and lower dose to surrounding structures by the dosimetric characteristics. The dose measured at any point decreases with increasing the distance between the source and point of measurement due to rapid dose fall off property. The radioactive source is accurately transported from the remote after loading system to the catheter/applicator in the tumour site with high accuracy in brachytherapy [1]. In the treatment of lung carcinoma, EBBT is well-established modality with high response rates [2,3]. EBBT is used in the treatment of bronchogenic carcinoma curatively. EBBT is used either alone or in combination with external beam radiotherapy [4,5]. A worldwide American Brachytherapy Society (ABS) recommends the guidelines for brachytherapy treatment. The ABS suggests that when brachytherapy is used for the palliation, as a sole modality for treatment, the dose fractionation schedule is 7.5 Gy per fraction for three fractions, 10 Gy per fraction for two fractions or 6 Gy per fraction for four fractions with one week gap in between the fractions [6]. The dose must be prescribed at 1 cm radius from the catheter center in EBBT for the treatment length [7]. One another dose prescription method is to the bronchial mucosa segment within the target after measuring the tracheobronchial airway [8]. There may be under dose at the proximal end and overdose at the distal end of the mucosa on the target. In the latter method where the dose prescribed at mucosa then a condition of overdose arises, if catheter is in close contact with the mucosa. On the plain radiograph, the detailed dosimetric analysis is not possible. Hence, important dosimetric information is collected with the CT scan in brachytherapy [9]. EBBT planning in the lung carcinoma is performed on the CT data set of the patient with the lumencare 6F catheter inserted in the bronchus where the radiation dose to be given. The radiation dose to the tumour is delivered in the HDR after loading brachytherapy machine (microselectron HDR) with Ir-192 radioactive source. The TV is covered with the prescribed dose and OARs doses are evaluated at the time of plan approval in TPS. The

brachytherapy treatment procedure time can be reduced by starting the treatment without any delay if standard doses and lengths are used. The treatment planning time is feasibly reduced when one catheter is used with minimal curvature in the irradiated area and by applying precalculated standard treatment plans for 3-10 cm tumour length with the 5-10 Gy dose prescribed at 1 cm from the source centre with equal dwell times [10].

Present study is novel as there is no literature published in this field of knowledge as authors carry out an exhaustive literature search in this area. The present study of volumetric and dosimetric evaluation in EBBT was done to analyse the effect of tumour location in the bronchus, tumour site, and TV on OARs doses in EBBT treatment.

MATERIALS AND METHODS

This was a cross-sectional study conducted in the Radiation Oncology Department Cancer Research Institute, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University Dehradun, Uttarakhand, India, on patients of lung carcinoma from January 2018 to December 2020. Ethical Clearance from the Institutional Ethical Committee (IEC) with approval number SRHU/HIMS/E-1/2023/54 was obtained.

Inclusion criteria: Patients with carcinoma of the lung with the endobronchial tumour in the primary and secondary bronchus were included in the study.

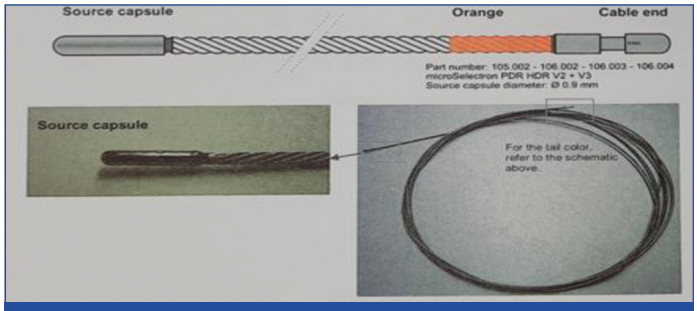
Exclusion criteria: Patients with tumour in the plural and peripheral part of the lung other than primary and secondary bronchus were excluded from the study.

Patient selection: Purposive and convenient sampling was done due to the limitation of the patients. Total 30 patients with lung carcinoma were equally distributed in two groups for left and right lung carcinoma. The two groups were further divided into two subgroups, in each main group for tumour location in the lower and middle bronchus region where again almost equal numbers of patients were included. In the subgroups, eight patients were lower bronchus lesions and seven patients were middle bronchus lesions in either side of the lung carcinoma. As per the TV, 30 patients with different TV were classified into two groups TV <22 cc and TV >22 cc.

Endobronchial Brachytherapy (EBBT): Bronchoscopy was performed prior to EBBT to evaluate the tumour location, size, and obstruction under local anaesthesia. The bronchoscopic findings were used to determine the TV. The upper and lower margin of the TV was taken very carefully. In a completely obstructive lesion, the distal margin through endoscopy was not possible. The lumencare 6 French (6F) catheter was inserted through the brush channel of the bronchoscope into the tumour. A dummy source X-ray marker was positioned in the catheter which was inserted into the bronchus to visualise the catheter in the CT images. A source position simulator instrument tool was used to determine the length of the catheter and check for any obstruction in the catheter prior to the CT scan. The study was based on the CT scan data of the patient so there were no premedication/anaesthetic procedures required.

Treatment planning: The patient CT scan was obtained with 2-3 mm axial CT slice with a dummy source and exported to the TPS (Oncentra Master Plan V3.3; Nucletron Pvt., Ltd.,) through "DICOM" local area networking system for treatment planning. The length, lateral and vertical extension of the tumour volume and OARs was delineated by the radiation oncologists on the CT data set. The accurate TV definition and volumetric dose information were possible with CT scan-based planning which can improve the brachytherapy therapeutic ratio [9].

The catheter was reconstructed by medical physicists. The dwell positions were selected to cover the endobronchial tumour volume and the additional margin was taken on distal and proximal ends. The dose per fraction was used 7 Gy prescribed at 1 cm from centre of the catheter for treatment length including 2 cm margin at both the ends as per the ABS guidelines for brachytherapy treatment in lung carcinoma [6]. The optimised EBBT plan was exported to the microselectron HDR V3 remote after loading unit (Nucletron Pvt., Ltd.,) for treatment execution. The Ir-192 HDR source has a source capsule length 4.5 mm and diameter of 0.9 mm in the HDR unit [Table/Fig-1] [11].



[Table/Fig-1]: High-dose-rate 192Ir brachytherapy source capsule design.

Three EBBT sessions were given to each patient and three CT scan set of every patient taken for the treatment purpose. The first session, second session and third session CT data set was named as $CT_{1\#}$, $CT_{2\#}$ and $CT_{3\#}$ in each patient, respectively. The TV and OAR were delineated in the CT scan of the patient by radiation oncologists. The dosimetric and volumetric analysis was performed on all the patient's plans. The total doses to OARs in three EBBT session and effect of TV, tumour site and tumour location on OARs doses were recorded from the DVH and detail table tool from the plan analysis window in TPS in each patient.

STATISTICAL ANALYSIS

Interpretation and analysis of the results obtained were carried out using SPSS statistics version 22.0 software (IBM Corp., Armonk, N.Y., USA) and MS Excel spreadsheets. The means of the doses were compared by the parametric independent-samples t-test and it was statistically significant by $p<0.05$.

RESULTS

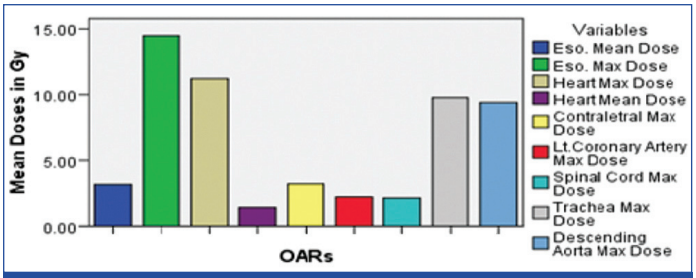
Thirty patients of lung carcinoma with mean age 63.1 years with male (N=28) to female (N=2) ratio of 14:1. Ninety EBBT sessions of 30 lung carcinoma patients were assessed for dosimetric as well as volumetric evaluation after the completion of treatment. The dose and volume parameters in the first session of brachytherapy were made the reference or base values for assessment of effects after second and third sessions of brachytherapy in each patient.

Dosimetric analysis: The average maximum doses to oesophagus, heart, contralateral lung, left coronary artery, spinal cord, trachea and descending aorta were 14.48, 11.22, 3.21, 2.22, 2.14, 9.77 and 9.4 Gy and average of the mean dose to oesophagus and heart were 3.18 and 1.42 Gy in three EBBT sessions, respectively [Table/Fig-2].

The mean dose difference between left and right lung tumour site were analysed, the mean dose to the oesophagus and maximum dose to the oesophagus, contra-lateral lung, Lt. coronary artery and descending aorta were significantly higher in the left lung compared to right lung, respectively [Table/Fig-3].

The maximum dose to the contra-lateral lung and spinal cord were significantly higher in middle-lower bronchial lesion with p-value 0.024 and 0.023, respectively [Table/Fig-4].

Volumetric analysis: The volumetric analysis was performed on all the patients where the TV obtained from the TPS. The TV of 30 patients obtained from the TPS was classified in two groups as TV <22 cc and TV >22 cc for the analysis purpose and introduce



[Table/Fig-2]: Graph showing OARs mean doses received in three EBBT sessions.

a concept where tumour volume effect the doses to OAR in left and right lung lesion. In the two groups TV <22 cc and TV >22 cc, the patient's frequency was 14 and 16, respectively. The OARs doses were compared among these two TV groups for left and right-side lung tumour lesions. It was found that the OARs doses vary significantly in the group TV >22 cc among left and right-side lung tumour lesions whereas in the group TV <22 cc contralateral Lung max dose was found significant whereas rest of the OARs no significant variation found in left and right-side lung tumour lesion [Table/Fig-5,6].

S. No.	Organs At Risk (OAR)	Left lung mean dose (Gy)	Right lung mean dose (Gy)	Mean difference	p-value*
1	Oesophagus mean dose	3.7±1.65	2.57±0.70	1.20000	**0.015**
2	Oesophagus max dose	20.6±20.01	8.3±4.2	12.32333	**0.027**
3	Heart max dose	11.36±3.01	11.07±3.65	0.28800	0.816
4	Heart mean dose	1.50±0.33	1.33±0.60	0.17200	0.340
5	Contralateral lung max dose	4.61±2.75	1.80±1.31	2.81067	**0.001**
6	Lt. coronary artery max dose	2.71±1.20	1.70±0.56	1.00933	**0.007**
7	Spinal cord max dose	2.16±0.81	2.10±0.86	0.06333	0.839
8	Trachea max dose	10.29±4.18	9.23±4.70	1.06800	0.517
9	Descending aorta max dose	13.33±5.60	5.45±4.93	7.88533	**0.001**
10	Liver max dose	0.28±0.37	1.63±3.34	-1.35400	0.130
11	Kidney max dose	0.018±0.069	0.020±0.077	-0.00200	0.941

[Table/Fig-3]: Effect of tumour site on the doses to the Organs At Risk (OAR) in the EBBT sessions.
*Independent sample t-test was used for statistical analysis; p-value <0.05 is statistically significant

S. No.	Organs At Risk (OAR)	Lower region mean dose (Gy)	Middle-lower region mean dose (Gy)	Mean difference	p-value*
1	Oesophagus mean dose	3.17±1.70	3.18±0.98	-0.01018	0.984
2	Oesophagus max dose	9.94±5.57	19.65±21.17	-9.70857	0.088
3	Heart max dose	11.26±3.47	11.17±3.20	0.08991	0.942
4	Heart mean dose	1.43±0.59	1.40±0.33	0.02661	0.884
5	Contralateral lung max dose	2.24±1.46	4.31±3.10	-2.07357	**0.024**
6	Lt. coronary artery max dose	2.01±1.46	2.44±1.37	-0.42768	0.277
7	Spinal cord max dose	1.82±0.68	2.49±0.85	-0.67643	**0.023**
8	Trachea max dose	8.72±3.48	10.95±5.14	-2.23723	0.170
9	Descending aorta max dose	9.19±6.78	9.63±6.53	-0.43750	0.859
10	Liver max dose	0.45±0.94	1.53±3.39	-1.07438	0.235
11	Kidney max dose	0.00±0.00	0.04±0.10	-0.04071	0.126

[Table/Fig-4]: Effect of tumour location on the doses to the Organs At Risk (OAR) in the EBBT sessions.
*Independent sample t-test was used for statistical analysis; p-value <0.05 is statistically significant

S. No.	Organs At Risk (OAR)	Mean±SD (Doses in Gy)		Mean difference	p-value*
		Left lung	Right lung		
1	Oesophagus mean dose	3.43±1.69	2.33±1.13	-1.6229167	**0.002**
2	Oesophagus max dose	15.70±20.86	7.00±9.82	-11.7329167	**0.008**
3	Heart max dose	11.04±3.41	10.89±3.97	-0.9029167	0.671
4	Heart mean dose	1.54±0.62	1.25±0.39	-0.4179167	**0.027**
5	Contralateral lung max dose	3.32±3.21	1.57±1.72	-2.2716667	**0.003**
6	Lt. coronary artery max dose	3.17±0.58	1.67±1.47	-1.9716667	**0.006**
7	Spinal cord max dose	2.07±0.62	2.33±0.97	-0.2175000	0.638
8	Trachea max dose	8.78±3.29	6.30±4.52	-2.6304167	0.253
9	Descending aorta max dose	13.77±5.76	2.92±6.54	-13.1820833	**0.001**
10	Liver max dose	0.36±0.96	2.38±041	0.7058333	0.291
11	Kidney max dose	0.03±0.08	00.00±0.09	-0.04500	0.264

[Table/Fig-5]: Effect of tumour volume TV >22 cc on the doses to the Organs At Risk (OAR) in the EBBT sessions.
*Independent sample t-test was used for statistical analysis; p-value <0.05 is statistically significant

S. No.	OARs	Mean±SD (Doses in Gy)		Mean difference	p-value*
		Left lung	Right lung		
1	Oesophagus mean dose	4.16±2.13	2.84±0.81	-0.7574603	0.364
2	Oesophagus max dose	26.27±27.43	9.81±5.71	-11.8620635	0.242

3	Heart max dose	11.72±1.56	11.28±4.76	0.3914286	0.804
4	Heart mean dose	1.46±0.25	1.43±0.87	0.0450794	0.884
5	Contralateral lung max dose	6.09±0.37	2.07±1.86	-3.0736508	**0.046**
6	Lt. coronary artery max dose	2.19±0.49	1.74±0.61	-0.3088889	0.225
7	Spinal cord max dose	2.27±0.68	1.84±0.52	0.0493651	0.725
8	Trachea max dose	12.03±3.23	12.57±3.58	0.9614286	0.677
9	Descending aorta max dose	12.83±4.77	8.34±6.12	-3.1242857	0.277
10	Liver max dose	0.18±0.32	0.77±3.31	1.9987302	0.227
11	Kidney max dose	0.00±0.00	0.04±0.11	0.0428571	0.271

[Table/Fig-6]: Effect of tumour volume TV <22 cc on the doses to the Organs At Risk (OAR) in the EBBT sessions.
*Independent sample t-test was used for statistical analysis; p-value <0.05 is statistically significant

The sum of OARs doses in first, second and third session of brachytherapy was calculated and compared the doses in different groups which were made as per the tumour lesion site, location and TV. The results showed that the tumour location in the lungs, tumour site in left and right lung and TV >22 cc and TV <22 cc affect the doses to OARs in brachytherapy treatment of lung carcinoma patients.

DISCUSSION

As per the literature many studies are found related to the clinical point of view and on the outcome of the brachytherapy treatment on the relief of symptoms and improved quality of life of the patient post-treatment [10]. As the work related to this study is not performed earlier so no data is available to compare the dosimetric and volumetric findings. Dhillon S et al., observed the endoscopic response at one-month post-treatment in 84% of patients and more than 50% endobronchial component reduction in 15 patients [12]. In this situation, immediate priority is given to remove the blockage in the bronchus to clear the airway path of the patient [13,14]. Gustafson G et al., reported that the degree of obstruction was reduced by around 50% or greater in 64% of their patients [15]. This reduction in the obstruction can be related with the tumour volume, which affects directly the doses to the OAR in three consecutive EBBT sessions in the included patients. As the OAR doses in the other sites like carcinoma cervix and oesophagus were analysed by the authors whereas, in the EBBT, the dosimetric and volumetric analysis was not found in the literature available.

Singh DP et al., prescribed the dose at 0.8 cm distance instead of 1 cm distance from the centre of the catheter by measuring the distance between the mucosa and catheter in the CT scan of the patient. The dose coverage to the endobronchial lesion was adequate in this [16]. The normal transfer tube used in the EBBT placed eccentrically in the bronchial lumen for irradiation leads to a high dose on the bronchial mucosa. Omori K et al., developed an applicator with two wings that open at the radiation delivery location and maintain the source in the centre of the lumen to minimise the radiation dose to the bronchial mucosa. They reported that by using this applicator the haemoptysis and bronchial stenosis were less in EBBT [17]. Sur R et al., did a randomised trial study and found that there was a moderate improvement in the relief of symptoms by combining the two treatment modalities like EBBT and EBRT but the improvement was not statistically significant [18].

Brachytherapy can be a choice of treatment in lung carcinoma depending upon the location of the tumour lesion. The tumour volume affects the doses to the OAR and tumour volume coverage with prescribed dose. Large tumour volume showed the increased doses to OARs. The strength of the study was to explore the factors affecting the doses to the OAR in lung carcinoma brachytherapy. Results of this study can be helpful in the selection of the patient for brachytherapy treatment. This treatment option is fast to perform, not very expensive, and can be performed on an outpatient basis.

On the basis of observed findings, it can be stated that EBBT provides effective palliative treatment and should be recommended to patients with endobronchial tumour lesions.

Limitation(s)

The limitation of the study was relatively small cohort/sample size because the EBBT technique is not regularly performed and the patients with tumour located only in the major bronchi were included in the study because the patient selection for EBBT is very important. The study included the doses to OAR calculated by the TPS only which were not validated in the study by any other experimental dosimetric method in the lung carcinoma EBBT technique.

CONCLUSION(S)

The OARs doses were higher for a large-volume tumour in the middle-lower region than small volume tumour in the lower region in the bronchus while the OAR tolerance dose limit was not exceeded. The OARs doses were higher in left lung carcinoma than in right lung carcinoma patients. The effect of TV on the OARs doses was significant for TV >22 cc and contralateral lung max dose was found significant whereas rest of the OARs no significant variation found for TV <22 cc in left and right-side lung lesions. Hence, the EBBT is a very effective treatment modality in lung carcinoma with the best selection of the patient considering the tumour location and site to achieve an optimised plan with good quality of life.

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PARTICULARS OF CONTRIBUTORS:
1. Ph.D. Research Scholar (Medical Physics), Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
2. Professor, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
3. Assistant Professor, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
4. Professor, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
5. Assistant Professor, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
6. Lecturer, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
7. Professor, Department of Radiation Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.
8. Professor, Department of Surgical Oncology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Mr. Ravi Kant,
Ph.D. Research Scholar (Medical Physics), Department of Radiation Oncology,
Himalayan Institute of Medical Sciences, Swami Rama Himalayan University,
Jolly Grant, Doiwala, Dehradun-248016, Uttarakhand, India.
E-mail: ravikantphy@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 23, 2023
- Manual Googling: Mar 03, 2023
- iThenticate Software: Apr 15, 2023 (2%)

ETYMOLOGY: Author Origin

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- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA (Research work was not related directly to the patient)
- For any images presented appropriate consent has been obtained from the subjects. NA

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