Phase Angle Research Study in Neoplastic Patients Treated with Standard Chemotherapy (PARSNIP)

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Abstract

Purpose

This study evaluated whether a series of analyses that are associated with physical state decay, such as phase angle (PhA), obtained by bio-electrical impedance analysis (BIA) performed before the first cycle (t0) and after 1-2 months (t1) of chemotherapy, might be associated with differences in a series of clinical factors.

Methods

In this monocentric, prospective, observational study we enrolled patients affected by solid tumors (breast or gastrointestinal cancers) treated with chemotherapy at our Institution between February and July 2019. We calculated whether a series of clinical factors (age, sex, type of chemotherapy regimen, metastatic vs not-metastatic disease involvement and different tumor type) might be associated with changes in PhA. BIA analysis was performed with DF50 Body Composition Analyzer. Statistical analysis was performed with statistical software R (4.1.0) and MedCalc® Statistical Software version 19.7.2.

Results

Thirty patients were enrolled, treated with chemotherapy in neoadjuvant, adjuvant or first line metastatic setting. In the whole cohort of patients, it was observed a reduction of PhA ($p=0.02$) between t0 and t1. Stratifying by clinical variables, female patients ($p=0.02$), younger patients ($p=0.02$), predominantly with not-metastatic involvement ($p=0.03$), affected by breast cancer ($p<0.01$) and who received taxane-based chemotherapy ($p=0.01$) were those a statistically significant difference in PhA between t0 and t1 was observed.

Conclusion

Our study suggest that PhA decrease is frequent as neoplastic disease worsens. BIA is an effective method for detecting PhA that seems to be a good indicator of patient's malnutrition state. Selected subgroups of patients might be at higher risk of PhA decrease (females, breast cancer patients, younger patients, those treated with taxanes) and should be offered prompt nutritional assessment and support. Further studies in these subgroups of patients are recommended.

1. Introduction

Incidence and mortality of cancer are globally increasing; according to estimates from the International Agency for Research on Cancer (IARC), in 2018 there were 17.0 million new cancer cases and 9.5 million cancer deaths worldwide [1]. By 2040, the global burden is expected to grow to 27.5 million new cancer

cases and 16.3 million cancer deaths simply due to aging and human population growth [2]. It is estimated that 2 out of 5 people will likely develop cancer as its lifetime risk is approximately 40% [3]. This estimation is set to increase with the improvement of the social-economic status of the population, which also means greater life-expectancy and increased median age of the population.

Cancer diagnosis has a huge impact on patients' lives, both from a physical/symptomatological and psycho/social point of view. In addition to that, the increased use of drugs and medications required to counteract symptoms of the underlying disease might also have meaningful side effects, worsening patients' quality of life and performance status [4].

Also, cancer patients are particularly at high risk for malnutrition which is defined as the nutritional status wherein a shortage of energy, proteins and other nutrients causes adverse side-effects measurable on tissues, functions, and clinical outcome [5]. Malnutrition in cancer patients is due both to the disease itself and to the side effects of therapies which can in turn negatively affect either the response to therapy and/or the QoL of patients [6].

Malnutrition establishes a partially reversible process leading to pre-cachexia and finally to cachexia and sarcopenia. Cachexia is a multifactorial condition characterized by unintentional weight loss associated to skeletal muscle mass loss, with or without fat mass loss [7]. It is frequently present in advanced illness and occurs in about 80% cancer patients; in about 22-30% turns out to be the primary cause of death [8].

In recent years, the correlation between body composition (BC) and health status of cancer survivors has been extensively investigated [9–10–11]. In this sense, bioelectrical impedance analysis (BIA) has been found useful as it provides data on patients' body composition and nutritional status, such as muscle mass and fluid status (balance of body water compartments). In fact, it is a bioelectrical method based on the assumption that electric current is well conducted by water and by human body parts containing electrolytes, but it is badly run by adipose tissue and bone mass [12].

BIA is a widely used, simple, reproducible, not expensive and not invasive method able to identify high-risk patients in clinical practice assessing accurately muscle mass [13].

Raw values, obtained by BIA, are resistance (R), reactance (Xc) and phase angle (PhA). BIA-derived PhA has been used as an alternative method to assess nutrition status and may be used as a predictor of clinical outcome as it is a marker of cells' health [14]. In particular, PhA is a rough estimate of cell membranes' integrity (related to electrical conductivity) and distribution of water at intracellular/extracellular spaces level [15]. High PhA values suggest good cell membranes status and thus optimal cellular functioning. Conversely, low PhA values have been associated with cell death and a progressive failure of cell membranes' function [16].

Facing this background, and in order to contribute to this field of knowledge, the present observational prospective study aims to evaluate changes in various parameters related to body composition, as measured using BIA, in patients with different solid tumors, before the first cycle of standard

chemotherapy treatment (t0), and about 1-2 months after t0 (t1). In particular, we focused on changes of PhA, in order to evaluate whether changes of this variable might suggest progressive decay of the physical state of the subjects under examination.

2. Patients And Methods

2.1 Patients

Thirty patients with either metastatic/locally advanced solid tumours who received chemotherapy were consecutively enrolled between February 2019 and July 2019. Their clinical characteristics are summarized in Table 1.

Table 1
Characteristics of enrolled subjects. Data are presented as Mean $\pm$ SD

	GI patients (n=14)	BC patients (n=16)	Tot patients (n=30)
Age (years)	61.5 $\pm$ 11.5	58.8 $\pm$ 10.9	60.1 $\pm$ 11.0
Gender (M/F)	6/8	0/16	8/22
BMI (Kg/m ²)	26.1 $\pm$ 4.9	24.7 $\pm$ 6.3	25.2 $\pm$ 5.5
Waist circumference (cm)	93.3 $\pm$ 13.5	83.1 $\pm$ 16.2	88.5 $\pm$ 15.6
MUAC (cm)	28.4 $\pm$ 4.2	26.7 $\pm$ 4.0	27.5 $\pm$ 4.1
BC=breast cancer; GI= Gastrointestinal;BMI=Body Mass Index; MUAC= Middle-Up Arm Circumference			

We decided not to include patients with lung cancer, melanoma, and hepatocellular carcinoma as the clinical management of these tumours involves frequently use of immunotherapy or target therapy rather than by chemotherapy.

No upper or lower age limits have been established, neither stratification factors have been considered due to the selected group homogeneity.

2.2 Methods

Height, weight, BMI, waist circumference, arm circumference, and BIA were measured to evaluate the nutritional status at enrolment (t0), and at time 1 (t1), that was 1-2 months after t0.

2.2.1 Anthropometric measurements

All anthropometric measurements were taken twice, and the average was recorded.

The weight of the participants was assessed using the standard beam balance and the scale was verified and calibrated at zero before each measurement. Participants' weight was measured after removing

heavy clothes and recorded to the nearest 0.1 Kg.

Height measurement of participants was taken using the standard measuring scale. Patients had to take off their shoes and to stand erect with their feet on a horizontal plane. The occiput, shoulder, buttocks, and heels touched the measuring board, and height was recorded to the nearest 0.1 cm.

Waist circumference was measured at the midpoint between the lowest margin of the last palpable rib and the top iliac crest while the patient is breathing and standing.

To measure the middle-up arm circumference (MUAC), the patient bent the right arm at 90° with the hand resting on the torso, whenever possible. Subsequently, the midpoint between the end of the olecranon prominence and the ulna was established, where the inelastic measuring tape was positioned around the arm and close to the skin, without pressing the soft tissue.

2.2.2 BIA

BIA analysis was performed with DF50 Body Composition Analyzer (ImpediMed DF50). Measurements were completed according to our previous study [17]. Briefly, the electrical resistance (R), reactance (Xc) and PhA for each patient was recorded, and body compartments after adjusting for age, sex, weight and height were estimated. Measurements were made in supine position with 4 conventional electrodes: 2 on the wrist and 2 on the ipsilateral foot. Patients were advised as not to have food or drink intake in the previous 4 h, no exercise in the previous 12 h, an empty bladder and removal of jewellery and clothes with metallic elements, before testing.

R and Xc values were included in a specific program and were processed in order to obtain the Biavector graphic, which allows to realize a quick nutritional status evaluation. In detail, the data obtained thanks to this procedure are cell mass (BCM), total water (TBW), extracellular water (ECW), intracellular water (ICW), fat mass (FM), lean mass (FFM), basal metabolism (MB), body mass index (BMI), and body cell mass index (BCMI).

2.2.3 Statistical considerations

Statistical analysis was performed using the statistical software R (4.1.0) and by MedCalc® Statistical Software version 19.7.2 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2021).

Results are expressed either as Means±SD or Median±SD. Differences in PhA based on clinical factors at t0 and t1 were assessed by Mann-Whitney test, whereas changes in PhA values between t0 and at t1 were assessed by Wilcoxon test. Factors that were taken into account for further calculations were: sex (male vs female), age (<70 or ≥70 years old at study entry), metastatic disease vs not metastatic disease, cancer type (breast cancer vs gastrointestinal cancer) and type of chemotherapeutic treatment received. All patients had to perform at least one nutritional and BIA assessment as to be considered eligible for further analyses.

A p-value < 0.05 was deemed as statistically significant.

3. Results

3.1 Patients Population

Between February 2019 and July 2019, 87 consecutive patients that were admitted at Oncology Clinic, Università Politecnica delle Marche were screened. Fifty-seven were excluded based on exclusion criteria. Characteristics of the remaining 30 patients are shown in Table 1.

16 out of 30 patients were affected by breast cancer. All breast cancer patients were female and all of them did not have metastases at the time of study entry. All these patients received chemotherapy as either adjuvant/neoadjuvant treatment. The remaining 14 enrolled patients (6 males and 8 females) showed metastatic/locally advanced gastrointestinal cancer (gastric/rectal-colon/pancreatic/bile ducts).

At the study entry, 50% had metastases, and thus received palliative chemotherapy, while the rest had a locally advanced disease treated with surgery followed by adjuvant therapy.

3.2 Results for the entire cohort

Table 2 shows changes that occurred from baseline (t0) to final measurement (t1) in the whole cohort.

Table 2: changes in body composition of BC patients. Data are presented as for median value of the distribution (and interquartile range)

BMI=Body Mass Index; MUAC= Middle-Up Arm Circumference; FFM=Free Fat Mass; FM= Fat Mass; ICW= IntraCellular Water; ECW: ExtraCellular Water; TBW= Total Body Water; PhA=Phase Angle.

ALL Patients	t0	t1	p
BMI (kg/m ²)	24.45 (20.50-28.70)	24.5 (20.40-28.10)	0.23
Waist circumference (cm)	89 (74-97)	89.50 (72.50-99)	0.46
MUAC (cm)	26.25 (24.50-31)	26.50 (24-30.50)	0.54
FFM (%)	67.90 (60.40-72.95)	68.50 (64.05-74.95)	<0.01
FM (%)	32.10 (27.05-39.60)	31.50 (25.05-35.95)	<0.01
ICW (%)	49.70 (44.32-51.52)	47.20 (44.52-50.25)	0.08
ECW (%)	51 (48.02-56.05)	52.8 (49.60-55.72)	0.04
TBW (%)	49.65 (44.20-52.75)	50.20 (46.45-54.30)	0.03
PhA (°)	5.10 (4.45-5.70)	4.85 (4.25-5.25)	0.02

As already stated all patients performed at least one nutritional and BIA assessment whereas only 24/30 (80%) performed both t0 and t1 assessment.

It was observed a trend towards a reduction of ICW percentages between t0 and t1, albeit it was not statistically significant ($p=0.08$). On the other hand, ECW increased significantly between t0 and t1 ($p=0.04$). In addition to that, PhA decreased significantly between t0 and t1 ($p=0.02$) (Table 2).

Furthermore, while BMI ($p=0.23$) and both waist circumference ($p=0.46$) and MUAC ($p=0.54$) were not significantly different between t0 and t1, fat-free mass was significantly increased ($p<0.01$) and conversely fat mass was significantly lowered ($p<0.01$) between t0 and t1.

Figure 1 shows body composition changes as boxplot in ICW (panel A), ECW (panel B) and PhA (Panel C).

3.3. Results stratified by variables.

We assessed the impact of different variables on changes of PhA.

As already stated, 8/30 patients were male and the remaining 22/30 patients were female. There were not statistically significant differences in terms of PhA at t0 ($p=0.47$) or PhA at t1 ($p=0.41$) between the two groups. When assessing changes in PhA in the male population, it was not demonstrated a statistically significant difference in PhA between t0 and t1 ($p=0.40$). In females, however, a statistically significant difference between PhA changes between t0 and t1 was seen ($p=0.02$). In particular, there was a decrease between t0 and t1 (median PhA value: 5.10 vs 4.70).

As for age stratification, 8/30 patients had age ≥ 70 years old, while the remaining 22/30 patients were younger than 70 years old. There was a statistically significant difference in terms of PhA at t0 between older patients vs younger patients ($p=0.03$). In particular, older patients had lower PhA values compared with younger patients (median PhA value: 4.55 vs 5.30). On the other hand, PhA at t1 was similar between older and younger patients (median PhA value: 4.90 vs 4.95, $p=0.47$). When assessing changes in PhA in older patients, it was not demonstrated a statistically significant difference in PhA between t0 and t1 ($p=0.57$). In younger patients, a statistically significant difference was seen comparing t0 and t1 ($p=0.02$). In particular, decreased PhA was observed between t0 and t1 (median PhA value: 5.25 vs 4.80).

Metastatic vs not-metastatic disease seemed to have an impact on PhA: albeit PhA levels at t0 were not significantly different between patients with metastatic disease ($p=0.09$) and similarly also PhA levels at t1 were not significantly different ($p=0.37$), when we analysed changes in PhA between t0 and t1, patients with metastatic disease did not have any change in PhA values ($p=0.40$), while in not-metastatic disease there was a statistically significant difference in PhA between t0 and t1 ($p=0.03$). In particular, median PhA value was decreased from t0 to t1 (5.20 vs 4.95).

Tumor type seemed to have an impact on differences in PhA: t0 levels of PhA were significantly lower in GI cancer patients compared with breast cancer (respectively, median PhA 4.60 vs 5.45, $p=0.03$). On the other hand, t1 levels of PhA were not significantly different ($p=0.50$). Indeed, in GI cancer patients, PhA was not significantly different between t0 and t1 ($p=0.60$). On the other hand, in breast cancer patients, PhA was significantly decreased between t0 and t1 (median PhA: 5.35 vs 4.85, $p<0.01$).

Finally, type of chemotherapy seemed to have also an impact on differences in PhA: even though we did not find any statistically significant differences between patients treated with taxanes (either paclitaxel, docetaxel or nab-paclitaxel) vs those who did not receive taxanes including chemotherapy regimens at t0 ($p=0.16$) and at t1 ($p=0.94$), patients who received chemotherapy which included taxanes had decreased PhA between t0 and t1 in a statistically significant fashion (median PhA: 5.20 vs 4.75, $p=0.01$). On the other hand, in patients who received other types of chemotherapy regimens which did not include taxanes, no statistically significant differences in changes in PhA were seen ($p=0.42$).

All these results are summarized in Figure 2.

4. Discussion And Conclusions

The present study evaluated body composition differences, assessed by BIA, in a prospective series of patients with breast and gastrointestinal cancer who received chemotherapy. In particular, our attention was focused on PhA. Overall, evidence of the literature reasonably supports the view that decreased PhA is frequently observed in cancer patients and PhA is correlated with QoL.

The use of BIA variables for evaluating nutritional status has increasingly gained attention, as cancer patients are extremely fragile individuals due to their gradual deterioration in health and due to side effects of drugs. Moreover, diminished physical performance affects individuals at psychological level, which in turn negatively affect the QoL: up to 85% of patients suffering from specific types of cancer (eg. pancreatic cancer) may be affected by malnutrition [18].

This condition may also be cause of asthenia, poor level of physical performance and poor individual functional outcome; it also can progress towards cachexia, an irreversible multifactorial syndrome, which accounts for 22-30% cancer deaths, and is associated with worse response to chemotherapy [19–20].

Metabolic shifts occurring during cancer and reduced physical activity determine loss of muscle mass, up to sarcopenia, which in turn may increase toxicity from chemotherapy and also represents a negative prognostic factor for post-surgical outcome [21–22–23]. For all these reasons, nutritional status evaluation in cancer patients has become a very important issue as it allows prompt identification of those patients affected by pre-cachexia, when the process leading to worsening of patients' conditions is still reversible.

In this sense, BIA has been found an easy-to-use, non-invasive method that provides information on patients' body composition and nutritional status, such as muscle mass and fluid status (balance of body water compartments) and can be easily repeated over time [24]. Among all indicators, obtained by BIA, one promising prognostic marker is PhA, which reflects cellular membrane integrity and hydration status. Typical PhA values in healthy individuals are comprised between 4 and 9 and it has already been described that PhA might be lower with increased age, female sex, lower BMI, and different disease states [25–26].

PhA has been studied in both oncologic and nononcologic patient, and lower values are constantly found associated with shorter survival [27]. In addition, measurement of PhA would seem a useful method for the detection/control of individuals at risk of malnutrition and for the evaluation of the QoL of cancer patients [28–29–30].

In our present study, patients with breast and gastrointestinal cancer were taken into consideration in terms of anthropometric measurements such as BMI, waist and arm circumference, and BIA with special focus to PhA, at t0 (the beginning of chemotherapy) and at t1 (1-2 months after t0).

No significant differences regarding changes in BMI in both groups were found. Despite previous studies have suggested that chemotherapy might also determine changes in patients' BMI, we believe that our results more closely reflect the fact that BMI is a poor estimator of body composition: indeed, other variables such as ECW and ICW underwent more marked changes during the course of chemotherapy, thus supporting the idea that these variables should be assessed more carefully instead of BMI [31]. Indeed, in the present study, an increase in ECW and a decrease in ICW from t0 to t1 was observed, as a sign of collapse in fluid balance system, related to malnutrition.

In addition to these findings, a substantial PhA reduction from t0 to t1 was highlighted, as to suggest progressive loss of cells structural integrity, which is shown with the impairment of patients' physical conditions. Our results are in accordance with those by Martins et al. [32] showing that higher PhA values are related to higher ICW values and to the maintenance of ECW/ICW ratio, suggesting the highest quality and the integrity of the cellular membrane. Optimal cut-off for PhA has already been proposed as values lower/greater than 5.6 [33]. Our results showed that baseline levels of PhA were lower than this pre-defined cut-off in most patients who had gastrointestinal cancer and in older patients. In addition to that, even in those patients who presented with higher baseline levels of PhA upon treatment start, they mostly presented with decreased levels after only 1-2 months of treatment.

Focusing on gastrointestinal cancer patients, we also observed FFM increase associated with FM decrease, and an increase in TBW, as well as increased ECW. All these changes are usually associated with increased basal metabolic rate (BMR) due to cancer. In fact, it is well documented how the reprogramming of energy metabolism is one of the key features of cancer and metabolic transformation is a central event in tumorigenesis [34]. Another hypothesis that might explain such changes might be due to increased lipid catabolism due to proinflammatory cytokines released by cancer [35]. It must be noticed, however, that we failed to demonstrate a statistically significant difference between metastatic and not-metastatic patients, thus lessening the potential impact of this factor as cytokines release should be obviously greater in patients with metastatic involvement compared to those without metastases.

When comparing the two groups of cancer patients, at t0, higher ICW percentage has been observed in breast cancer patients compared to GI cancer patients, while ECW was higher in GI cancer patients, possibly due to their diminished digestive capacities. Our results further highlight the importance of monitoring dietary intake of GI cancer patients, which may not be fully ascertained by some malnutrition screening tools. Indeed, despite there is an increased consensus on the importance of prompt recognition

of changes in dietary intake in patients with gastrointestinal malignancies, there is still the need for improvement on this matter [36].

Overall, evidence of the literature reasonably supports the view that widespread malnutrition can be found in patients with GI malignancies, though it remains an underdiagnosed problem in cancer patients [37–38].

Our results show that at t0, lower PhA levels in GI cancer patients, compared to patients with breast cancer, were observed and, as mentioned before, low phase angle suggests cell death or decreased cell integrity, whereas higher phase angle suggests healthy cell. On the contrary, at t1, PhA values were not significantly between the two groups. In addition to that, we failed to show any significant change in PhA values in GI cancer patients between t0 and t1, whereas in BC patients a considerable reduction in PhA values between t0 and t1 was observed, suggesting that in this selected group of patients there might be a greater susceptibility to the damaging effects of chemotherapy.

This last data is in agreement with those by Ramos da Silva et al [39]., which show significant differences in PhA before and after the beginning of the chemotherapy, suggesting that treatment related toxicities might have a negative impact on patient's prognosis.

In particular, more than due to the type of tumor or the clinical factors of the patient (age, gender), the factor that was mostly associated with decreased PhA was the use of chemotherapy regimens which included taxanes. Previous papers have highlighted the connections between proper cell membrane functioning and those proteins who made up the cell cytoskeleton [40]. Taxanes' mechanism of action is based on disruption of the tubulin polymerization mechanism; since tubulin is also one of the main proteins of the cytoskeleton, it can be hypothesised that changes in cell's cytoskeleton due to tubulin altered polymerization might lead to cell membrane damage and rupture, as suggested by PhA decrease.

There is a series of limitations to our study: first of all the small number of patients that precludes multivariate analysis to sort out the individual weight of each clinical factor on PhA changes. Moreover, hydration status is subject to severe changes during treatment in patients with cancer and thus, might have a impact on assessment performed by BIA; we tried to minimize individual measurement errors by advising patients to fast and to have an empty bladder before assessment but there might have been some instances such as in the case of presence of ascites, that might have had also an impact as confounding factor for this kind of analysis.

In summary, our data are in accordance with those present in the literature, suggesting that PhA decrease is frequent as the underlying neoplastic disease worsens. Our study suggests that younger female patients, affected by breast cancer more than by GI cancer and those patients who received treatment including taxanes, are at higher-risk of PhA decrease. BIA is an affordable, portable, easy-to-use, effective method for detecting PhA that seems to be a good indicator of the individuals' state of deterioration and malnutrition. Early recognition and intervention are critical to preserve nutrition status in patients with cancer and proceeding on the evaluation of this indicator could be beneficial. Further studies are

recommended in this specific subset of patients to increase the reproducibility and the usefulness of this tool in early recognition of malnourishment in cancer patients.

Abbreviations

BC	body composition
BCM	cell mass
BCMI	body cell mass index
BIA	Bio-Electrical Impedance Analysis
BMI	Body Mass Index
BMR	basal metabolic rate
ECW	extracellular water
FFM	lean mass
FM	fat mass
G-CSF	Granulocyte-colony stimulating factor
GI	Gastrointestinal
GPCR	G Protein-coupled receptor
ICW	intracellular water
IARC	International Agency for Research on Cancer
MB	basal metabolism
MSG	Monosodium glutamate
MUAC	middle-up arm circumference
NCI CTCAE	

PhA

phase angle

QoL

quality of life

R

resistance

TBW

total water

Xc

reactance

Declarations

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Code availability: All calculations that have been performed as to achieve the results that are contained in this research paper have been performed by using R statistical software (ver. 4.1.0) and Medcalc (version 19.7.2 MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2021)

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Figures

Figure 1

shows body composition changes as boxplot in ICW (panel A), ECW (panel B) and PhA (Panel C).

Figure 1: percentage of body composition changes in the whole cohort. p-values refer to a comparison of body composition changes between t0 and t1. Panel A: percentages of ICW changes between t0 and t1 ($p=0.08$). Panel B: percentages of ECW changes between t0 and t1 ($p=0.04$). Panel C: PhA changes between t0 and t1 ($*p=0.02$)

Figure 2

Changes in Phase Angle measurements in patients selected by clinical factors.

Panel A: Changes in Phase Angle between T0 and T1 in female patients. Median PhA T0: 5.10 (range: 3.3-7.3, interquartile range: 4.77-5.55) vs median PhA T1: 4.7 (range: 3.5-5.9, interquartile range: 4.27-5.05). $p=0.0186$. Panel B: Changes in Phase angle between T0 and T1 in younger (<70 years old) patients. Median PhA T0: 5.25 (range: 3.30-7.30, interquartile range: 4.95-6.50) vs median PhA T1: 4.80 (range: 4.1-6.60, interquartile range: 4.30-5.40). $P=0.0146$. Panel C: Changes in Phase angle between T0 and T1 in patients with not-metastatic disease involvement. Median PhA T0: 5.20 (range: 4.10-7.30, interquartile range: 4.95-5.70) vs median PhA T1: 4.95 (range: 3.5-5.9, interquartile range: 3.50-5.90). $P=0.0299$. Panel D: Changes in Phase angle between T0 and T1 in patients with breast cancer. Median PhA T0: 5.34 (range: 4.1-7.3, interquartile range: 3.50-5.90) vs median PhA T1: 4.85 (range: 3.5-5.9, interquartile range: 4.40-5.35). $p=0.0029$. Panel E: Changes in Phase angle between T0 and T1 in patients treated with taxanes. Median PhA T0: 5.10 (range: 4.1-7.30, interquartile range: 4.77-5.72) vs median PhA T1: 4.70 (range: 3.50-5.90, interquartile range: 4.30-5.00). $p=0.0135$.

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