

Evaluation of the Predictive Validity of Thermography in Identifying Extravasation With Intravenous Chemotherapy Infusions

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ABSTRACT

Early detection of extravasation is important, but conventional methods of detection lack objectivity and reliability. This study evaluated the predictive validity of thermography for identifying extravasation during intravenous antineoplastic therapy. Of 257 patients who received chemotherapy through peripheral veins, extravasation was identified in 26. Thermography was performed every 15 to 30 minutes during the infusions. Sensitivity, specificity, positive predictive value, and negative predictive value using thermography were 84.6%, 94.8%, 64.7%, and 98.2%, respectively. This study showed that thermography offers an accurate prediction of extravasation.

Key words: antineoplastic agents, extravasation, thermography

Extravasation is one of the potential complications of intravenous infusions. The incidence of extravasation of antineoplastic agents has been reported as 0.01% to 0.6%.¹⁻³ The *Infusion Therapy Standards of Practice* defines extravasation as the “inadvertent infil-

tration of vesicant solution or medication into surrounding tissue.”^{4(p5149)} In particular, extravasation of antineoplastic agents can affect the skin and subcutaneous tissues as a result of the same cytotoxicity that makes these agents effective against cancer tissues, and is frequently cited as a

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cause of functional impairment, as well as ulceration, blistering, induration, and other cutaneous damage.⁵⁻¹⁰ Current measures to prevent extravasation include improved venipuncture techniques and placement of intravenous catheters at sites with a lower risk of movement.^{9,11-13} However, because the causes of extravasation also include tissue resistance and physical movement of the patient,^{9,10,14} preventing all forms of extravasation is difficult. And as the amount of extravascular leakage increases, cutaneous damage resulting from the extravasation of antineoplastic agents becomes less likely to heal.⁵ Thus, delays in detecting extravasation can lead to severe skin damage, making detection as early as possible crucial.

Clinical methods to diagnose extravasation are problematic because objectivity and reliability are currently lacking. Clinical diagnosis has previously been based on patients' accounts of pain and nurses' observations of erythema and swelling around the tip of the catheter.^{4,5,9-14} However, pain is influenced by an individual's pain threshold and potential impairments of perception, and it does not always accompany extravasation. Moreover, because pain and erythema also may occur as the result of drug-induced irritation of the vessel walls,⁹ cases are sometimes difficult to diagnose accurately. Such circumstances have given rise to the need for diagnostic techniques to identify extravasation that are both highly objective and reliable.

This research has focused on the use of thermography as a method of objectively assessing the presence of extravasation. Thermography is a noncontact, noninvasive modality that detects skin-surface temperature. While infusion solutions administered through indwelling vascular catheters are close to room temperature at approximately 25°C to 28°C, the temperature of the skin surface of humans typically is about 34°C to 36°C. This has led researchers to hypothesize that thermography could reveal this temperature difference and thereby make extravasation of infused solutions visible. A previous thermographic study by this research team took images of extravasation models using the arms of 6 healthy adult volunteers, which revealed a circular, low-temperature zone when extravasation occurred.¹⁵ However, this technique has not been validated in patients in clinical settings, and whether thermography can be used to diagnose extravasation in actual patients remains unclear.

The present study, therefore, sought to examine the validity of thermography in predicting extravasation following the administration of an antineoplastic agent by intravenous infusion and to demonstrate the limitations of thermography in diagnosing extravasation.

METHODS

Pilot Study

A pilot study was conducted to identify a diagnostic indicator for extravasation using thermography.

Participants and setting

The study population comprised 31 patients receiving chemotherapy in an outpatient setting and undergoing 34 treatments during a 1-month period at a university hospital.

Technique

Thermographic images of the area surrounding the infusion site were taken during chemotherapy at 15- to 30-minute intervals. On each patient's next hospital visit, the study investigator observed the skin around the infusion site and interviewed the patient.

Equipment

A Thermo Shot F30S system (Nippon Avionics, Tokyo, Japan) was used to obtain the thermographic images. The dimensions of the device are 100 mm (h) × 65 mm (w) × 45 mm (d), with a weight of 300 g. An uncooled microbolometer is mounted on the instrument. Infrared radiation from a specific range of wavelengths strikes the vanadium oxide or amorphous silicon component and changes its electrical resistance. This resistance change is measured and converted into temperatures that can be represented graphically. The detector resolution is 160 (h) × 120 (v) pixels, the spectral range is 8 to 13 μm, and the measurement range is -20°C to 100°C. The sensitivity is 0.1°C at 30°C, accuracy is ±2°C, and focal distance is 10 cm to infinity. The measurement results are displayed on a 2.7-inch liquid crystal display monitor.

During thermographic imaging, a 4°C difference between upper and lower temperatures was selected, and the temperature was adjusted as needed so that temperature variations could be visualized clearly, according to the environmental circumstances (temperature range, 28°C-32°C to 36°C-40°C).

The thermograph used in the present study was a compact device that can be positioned at the patient's bedside, making it easy for nurses to use in a clinical environment.

Data analysis

Extravasation was defined as swelling around the infusion site during administration, or as subcutaneous hemorrhage, erythema, pigmentation, induration, blistering, or epidermal loss occurring at any time before the next visit. Based on this definition, patients were assigned to either a nonextravasation group or an extravasation group. The properties of thermographic images from each group were then depicted using qualitative methods, with a focus on the respective similarities and differences.

Characteristics of thermographic imaging of extravasation

A total of 28 and 6 images were obtained from the nonextravasation and extravasation groups, respectively (Figure 1). A decline in skin temperature accompanying intravenous chemotherapy manifested as 3 patterns in the nonextravasation group. A low-temperature region along the vein

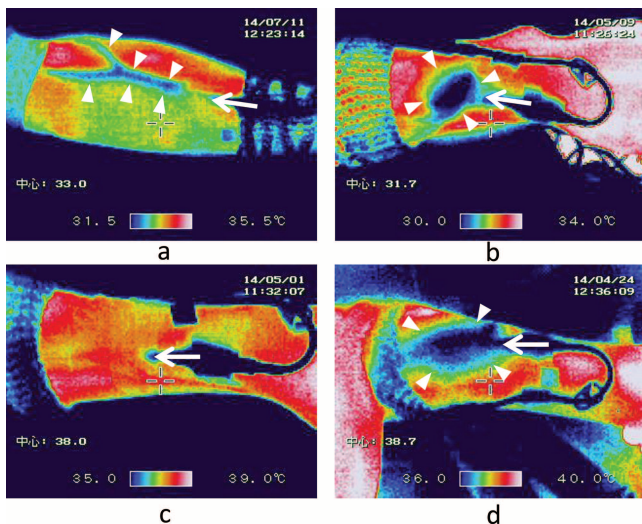


Figure 1 Classification of low-temperature regions in thermographic images: (a) low-temperature region running along the vein of a patient in the nonextravasation group; (b) low-temperature region expanding into perivenous tissue in a patient in the nonextravasation group; (c) image of a non-low-temperature region in a patient in the nonextravasation group; and (d) low-temperature region in a patient in the nonextravasation group. The decrease in temperature from the margin toward the center of the low-temperature region was minor. Δ : low-temperature region; \rightarrow : venipuncture site.

occurred in 15 treatments, and a locally expanding, perivenous low-temperature region occurred in 10 treatments. No low-temperature region occurred in 2 treatments. In the extravasation group, locally expanding, perivenous low-temperature regions were observed in all patients and were characterized by a gradual decrease in temperature from the margin to the center of the low-temperature region.

The findings of this pilot study showed that thermography can be used to detect extravasation-induced decreases in skin temperature in the clinical setting. Thermographic images in the extravasation group were characterized by a gradual decrease in temperature from the margin to the center of the low-temperature region. Based on this result, a temperature decrease in 1 cm of the margin of the low-temperature region was selected as the diagnostic indicator of extravasation. The objective of the present study was to examine the validity of temperature decreases on thermographic images for predicting extravasation.

Study 1: Predictive Validity of the Occurrence of Extravasation Using Thermography

Study design

This prospective cohort study examined the predictive validity of temperature decreases from the margin of the low-temperature region surrounding the tip of the infusion catheter as a diagnostic indicator for extravasation after thermographic imaging of the area around the insertion site during intravenous chemotherapy.

In this study, extravasation was defined as swelling around the infusion site during administration or as the appearance of subcutaneous hemorrhage, erythema, pigmentation, induration, blistering, or epidermal loss by the time of the next visit.

Participants and study setting

Study participants were patients who underwent treatment at the outpatient chemotherapy center of a university hospital between April 1, 2014 and September 30, 2014. The outpatient chemotherapy center had 13 beds and performed approximately 15 to 20 chemotherapy treatments a day. An infusion pump was used for all patients at this site. Patients were followed from the day of chemotherapy until the day of the next visit.

Subjects were patients who were undergoing chemotherapy administered through a peripheral vein, were at least 20 years old, and provided informed consent. Patients on chemotherapy regimens in which the administration of the antineoplastic agent was completed within 5 minutes, such as with a 1-time dose or bolus administration, were excluded from the study.

Procedure

Information on age, sex, body mass index (BMI), the disease, and medication history was obtained from the patients' medical records. Thermographic imaging during intravenous chemotherapy was performed by the study investigator. Thermographic images of the area surrounding the infusion site were the same as in the pilot study.

A 1-cm² plastic gauge was placed close to the base of the catheter to enable the accurate measurement of lengths in the images. The time taken for each image was less than 10 seconds. Nurses stationed in the outpatient chemotherapy center observed patients at 15- to 30-minute intervals for signs of erythema, swelling, pain, or discomfort around the infusion site. The diagnosis of extravasation based on macroscopic observation was performed by 2 nurses. Nurses stationed in the chemotherapy area and the investigator did not share observation findings with one another.

Pain, discomfort, induration, swelling, erythema, skin loss, blistering, fever, and subcutaneous hemorrhage were evaluated at the next hospital visit in accordance with the treatment schedule of the individual patient. These included symptoms observed by individual subjects at the next visit after administration.

Data analysis

Based on the study's definition of extravasation, patients were assigned to either the extravasation group or the nonextravasation group. Temperature decreases per 1 cm from the margin toward the center of the low-temperature region were calculated from the thermographic images. Regions displaying a $< 1^{\circ}\text{C}$ temperature difference between the surrounding skin temperature and the 30° arc along the vein were excluded from analysis. The minimum

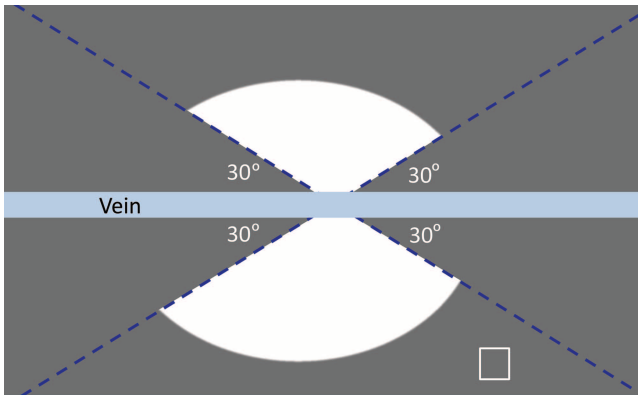


Figure 2 Measurement area of temperature decreases in the low-temperature region. Regions showing a temperature difference of $< 1^{\circ}\text{C}$ between the surrounding skin temperature and the area within a 30° arc alongside the vein were excluded from analysis; the white area only was measured. Surrounding skin temperature was defined as the mean temperature in an anatomically identical 1-cm^2 site unaffected by the infused solution. The smallest temperature decrease per 1 cm of this surrounding area was taken as the representative value.

temperature decrease value was selected from among all images taken during a single treatment and was used as the representative value (Figure 2).

Area under the curve (AUC) on a receiver operating characteristic (ROC) curve was calculated for temperature decrease per centimeter from the margin to the center of the low-temperature region on thermographic imaging and for the presence or absence of extravasation. Patients who did not exhibit any low-temperature regions were excluded from the calculation of AUC. Sensitivity, specificity, and positive and negative predictive values also were calculated for the classification of extravasation. The chi-square test was used to compare the extravasation detection rates of nurses and thermography. SPSS version 10.0 (IBM; Tokyo, Japan) was used for all statistical analyses.

Study 2: Limits of the Ability to Predict Extravasation Using Thermography

Study 2 was an observational study. Participants, the study setting, and the procedures followed were the same as in Study 1.

Data analysis

The following analyses were performed to identify limitations of the ability of thermography to determine extravasation. Analyses to determine vein path characteristics (confluences, bifurcations, and straightness) and whether the vein was located above a bone were performed based on the pilot study prediction that vein path and the location of bony prominences are related.

Confluence was defined as a thermographically confirmed confluence of veins within a 5-cm range from the catheter tip. *Bifurcation* was defined as a thermographically confirmed branching of veins within a 5-cm range from the catheter tip. *Straightness* was defined as the absence of confluences or bifurcations. *Directly above bone* meant

the low-temperature region was located at the bony prominence, because the catheter tip was located close to the bony prominence.

The ratio of vein path characteristics and vein location was compared between the positive and false-negative groups in the extravasation group.

The chi-square test was used to compare vein path characteristics and vein locations between the negative and false-positive groups in the nonextravasation group.

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki. All study procedures were reviewed and approved by the Clinical Studies Ethics Committee of Kanazawa Medical University (no. 239). After agreeing to the purpose of this study and signing the written informed consent form, data from subjects who participated in the study were used for analysis. If a nurse identified extravasation using conventional methods, administration of chemotherapy was discontinued immediately, and treatment was performed by a doctor and/or a nurse to prevent skin damage.

RESULTS

Participants

The study population comprised 104 patients who provided informed consent to participate in the study. The analysis set consisted of 80 of these patients (29 men, 51 women). The mean age was 64.7 ± 12.1 years, and mean BMI was $21.9 \pm 3.4 \text{ kg/m}^2$. Breast cancer was the most common underlying pathology (31 patients, 39%), followed by lung cancer (12 patients, 15%) and gastric and pancreatic cancer (9 patients each, 11%) (Table 1).

A total of 402 doses of chemotherapy were administered. Analysis was performed on 257 patients after excluding those with thermographic images of poor quality, those who could not be monitored until the end of treatment, those in whom skin observation could not be performed on the next visit, and those who developed phlebitis (Figure 3). The agents used were vesicants in 89 patients (35%), irritants in 108 patients (42%), and nonirritants in 60 patients (23%) (Table 2).

The infusion catheter was placed in the forearm in 201 patients (78%), followed by the dorsum of hand in 32 patients (12%) and the antecubital fossa in 12 patients (5%) (Table 2). The mean number of thermographic images taken during each treatment was 3.2 ± 1.6 , and the total number of images taken was 823. Mean infusion time per treatment was 85.2 ± 51.7 minutes, and mean time to next visit was 28.0 ± 19.0 days.

Extravasation was identified in 26 patients (10.1%). Mean room temperature on the day of the investigation was $25.3^{\circ}\text{C} \pm 0.6^{\circ}\text{C}$, and mean humidity was $57.0\% \pm 11.4\%$.

TABLE 1 Patient Disease	
Disease (n = 80)	n (%)
Breast cancer	31 (39)
Lung cancer	12 (15)
Gastric cancer	9 (11)
Pancreatic cancer	9 (11)
Lymphoma	4 (5)
Cholangiocarcinoma	4 (5)
Colorectal cancer	2 (3)
Other	9 (11)

TABLE 2 Treatment Characteristics: Antineoplastic Agents, Region		
		n (%)
Antineoplastic agents n = 257	Vesicant	89 (35)
	Irritant	108 (42)
	Nonirritant	60 (23)
Region n = 257	Forearm	201 (78)
	Dorsum of hand	32 (12)
	Antecubital fossa	12 (5)
	Brachium	6 (2)
	Wrist	5 (2)
	Other	1 (1)

Study 1: Predictive Validity of the Occurrence of Extravasation Using Thermography

Low-temperature regions were seen in all patients of the extravasation group and in 210 patients (91%) of the nonextravasation group. Mean temperature difference between the low-temperature region and surrounding area was $2.8^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$ for all patients, and $3.3^{\circ}\text{C} \pm 0.9^{\circ}\text{C}$ and $2.8^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$ in the extravasation and nonextravasation groups, respectively. Mean decrease in temperature at the margin of the low-temperature region was $1.4^{\circ}\text{C}/\text{cm} \pm 0.9^{\circ}\text{C}/\text{cm}$ for all patients, and $0.5^{\circ}\text{C}/\text{cm} \pm 0.3^{\circ}\text{C}/\text{cm}$ and $1.5^{\circ}\text{C}/\text{cm} \pm 0.9^{\circ}\text{C}/\text{cm}$ in the extravasation and nonextravasation groups, respectively.

Figure 4 shows typical thermographic images from the extravasation and nonextravasation groups. AUC was 0.94 (Figure 5). Based on a cutoff of $0.7^{\circ}\text{C}/\text{cm}$ as determined from the AUC for the ROC curve to maximize the positive predictive value and sensitivity, thermographic diagnosis of extravasation offered 84.6% sensitivity, 94.8% specificity, a positive predictive value of 64.7%, and a negative predictive value of 98.2% (Table 3).

Failure of nurses and thermographic imaging to detect extravasation occurred in 14 (54%) and 4 (15%) of the

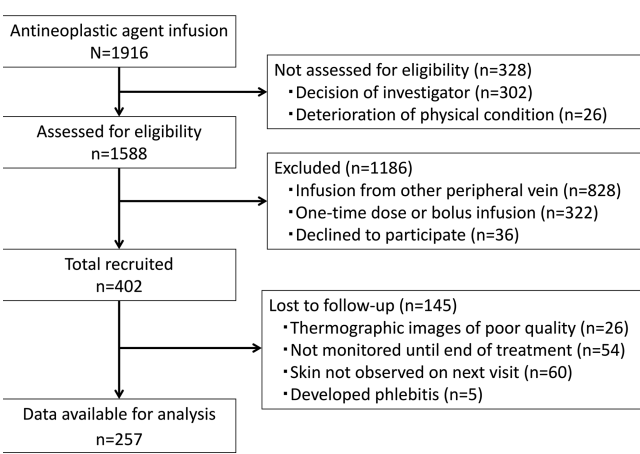


Figure 3 Flow of participants through the study.

26 extravasation cases, respectively, indicating a significantly higher detection rate for thermographic imaging ($P = .008$).

Study 2: Limitations of Thermography in Predicting Extravasation

In the nonextravasation group, vein features at the infusion site in false-positive cases were *straightness* in 1 patient (8.3%), *confluence* in 3 patients (25.0%), *bifurcation* in 3 patients (25.0%), and a combination of *bifurcation* and *confluence* in 5 patients (41.7%), indicating a significant difference between negative and false-positive groups ($P = .026$). The vein was located above a bony prominence

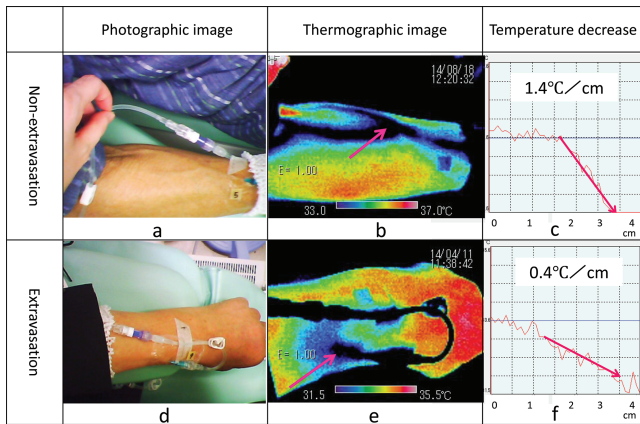


Figure 4 Thermographic images from patients in extravasation and nonextravasation groups. The figures represent typical thermographic images from patients in the extravasation and nonextravasation groups: (a) photographic image of a patient in the nonextravasation group; (b) thermographic image of the same patient in the nonextravasation group; (c) temperature decrease toward the center of the low-temperature region in the patient in the nonextravasation group ($1.4^{\circ}\text{C}/\text{cm}$); (d) photographic image of a patient in the extravasation group; (e) thermographic image of the same patient in the extravasation group; and (f) temperature decrease toward the center of the low-temperature region in the patient in the extravasation group ($0.4^{\circ}\text{C}/\text{cm}$). Thermographic imaging of extravasation featured a $< 0.7^{\circ}\text{C}/\text{cm}$ temperature decrease toward the center of the low-temperature region.

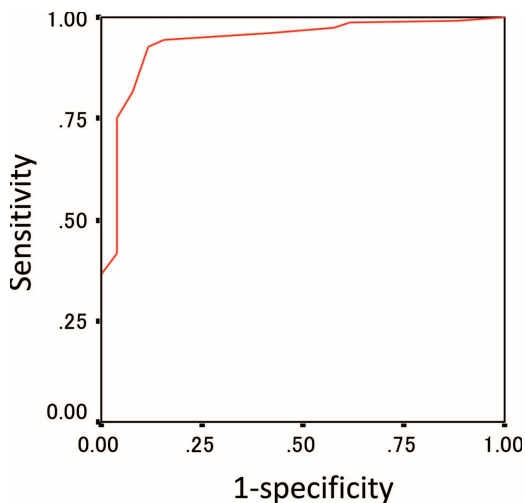


Figure 5 Receiver operating characteristic curve using temperature decrease per centimeter from the margin to the center of the low-temperature region on thermographic imaging as the diagnostic indicator of extravasation.

in 12 patients in the negative group (5.5%) and 3 patients in the false-positive group (25.0%), again indicating a significant difference between groups ($P = .008$) (Table 4).

In the extravasation group, 3 of 4 patients in the false-negative group developed sudden swelling during infusion, and 2 patients (50.0%) complained of pain. In the positive group, 6 patients developed swelling during infusion (27.3%), and 2 patients complained of pain (9.1%) (Table 5).

DISCUSSION

This study yielded 2 new findings. The first is that thermography allows highly accurate detection of extravasation, with 84.6% sensitivity, 94.8% specificity, a positive predictive value of 64.7%, and a negative predictive value of 98.2%. The second is that cases in which thermography was incapable of diagnosing extravasation were characterized by a combination of vein bifurcation and confluence, as well as the location of the vein over a bony prominence.

The AUC for thermographic detection of extravasation was 0.94. A decrease in skin temperature per centimeter from the margin toward the center of the low-temperature

region as seen on thermographic imaging is a capable diagnostic indicator of extravasation. Moreover, the optimal decrease temperature cutoff for diagnosing extravasation is $< 0.7^{\circ}\text{C}/\text{cm}$. Proper prevention of extravasation-induced skin damage requires accurate detection of extravasation, which, in turn, requires a high positive predictive value and sensitivity. The temperature yielding the highest positive predictive value was $0.6^{\circ}\text{C}/\text{cm}$. However, detection sensitivity at this temperature was very low, at just 57.7%, compared with that of other cutoffs. For this reason, a temperature of $< 0.7^{\circ}\text{C}/\text{cm}$ was selected as the optimal cutoff for assessing extravasation because of the high positive predictive value and sensitivity.

The gradual temperature changes seen at the margin of the low-temperature region in patients with extravasation could be attributed to the following factors. In intravenous infusion, the infused drug solution is rapidly diluted and does not remain at the area around the infusion site because of blood flow. For this reason, the low-temperature region on the skin surface tends to follow the path of the vasculature. When extravasation in subcutaneous tissue occurs, the infused drug solution is undiluted by blood and remains at the infusion site until spreading into and being absorbed by subcutaneous tissue, so the time until the temperature of the drug solution approaches that of the subcutaneous tissue is extended. Extravasation is presumed to be minor at first, before gradually spreading to the surrounding subcutaneous tissue, which is why the temperature change at the margin of the low-temperature region is presumed to be slow.

Symptoms resulting from irritants were considered unlikely to have been included in the extravasation group for 2 reasons. The first was the selection of subjects; the 5 patients who developed phlebitis were excluded from analysis in this study (Figure 3). The second reason involved the characteristics of the thermographic images. In this study, low-temperature areas appeared in all members of the extravasation group. Phlebitis caused by irritating drugs may show areas of high temperature, but low-temperature regions do not appear.

Thermographic diagnosis of extravasation also has limitations, and 2 primary types of diagnostic error were encountered. The first was a false-negative diagnosis seen in 4 chemotherapy treatments in which extravasation had

TABLE 3

Cutoff Points and Detection Rates for Extravasation Using Thermographically Revealed Temperature Decrease per Centimeter From Margin to Center of Low-Temperature Regions as an Indicator

Reduction Rate	Sensitivity	Specificity	PPV	NPV
$< 0.6^{\circ}\text{C}/\text{cm}$	57.7	96.5	65.2	95.3
$< 0.7^{\circ}\text{C}/\text{cm}$	84.6	94.8	64.7	98.2
$< 0.8^{\circ}\text{C}/\text{cm}$	88.5	93.9	62.2	98.6

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

TABLE 4**Characteristics of Catheter Tip Sites in the Nonextravasation Group (n = 231)**

		Negative	%	False Positive	%	P
Course of the vein	Straight	74	33.8	1	8.3	
	Confluence	46	21.0	3	25.0	
	Branch	53	24.2	3	25.0	
	Confluence and branch	23	10.5	5	41.7	
	Other	6	2.7	0	0.0	
	Unknown	17	7.8	0	0.0	.026 ^a
Bony prominence	Prominence	12	5.5	3	25.0	
	Nonprominence	207	94.5	9	75.0	.008 ^b

^aP value of vein path characteristics between the negative and false-positive groups.

^bP value of vein locations between the negative and false-positive groups.

occurred, but the thermographic image showed a sudden decrease toward the center of the low-temperature region. The second was a false-positive diagnosis seen in 12 treatments in which extravasation had not occurred, but the thermographic image showed a gradual decrease toward the center of the low-temperature region.

The fact that sudden swelling was macroscopically observed in 3 of the 4 false-negative cases suggests that for some unknown reason a large amount of the infused drug solution leaked into subcutaneous tissue more rapidly than in the other extravasation cases. Cases of extravasation characterized by sudden swelling cannot be accurately diagnosed by the method used in this study. However, the marked swelling meant that nurses could diagnose extravasation based on macroscopic observation. Because of this, thermography is not needed to diagnose extravasation characterized by sudden swelling.

On the other hand, false-positive cases in which extravasation did not occur but thermography showed a gradual decrease towards the center of the low-temperature region remain problematic from a clinical perspective. These false-positive cases were characterized by a combination

of vascular bifurcation and confluence and the location of veins over a bony prominence. With vascular bifurcations and confluences, the temperature of the drug solution flowing through the vein merges with that of blood in the vein, and depicts it as an extensive low-temperature region. In particular, sites at which veins bifurcate and join could give rise to intricately shaped margins detected as gently sloping low-temperature regions. When using thermography in a clinical setting, consideration should be given to the increased rate of false diagnosis; diagnosis, therefore, should be based on a combination of macroscopic observations and the symptoms patients complain of. Bony prominences are located away from the center of the body and, therefore, tend to show low temperatures regardless of the infusion. Intravenous infusion could lower the vein temperature around the bony prominence and, as a result, the temperature of the entire prominence, resulting in a thermographic image showing an extensive low-temperature region. The antecubital fossa and areas near bony prominences should be avoided when administering chemotherapy. As a result, problems would be caused rarely by the high false-positive rate at bone protrusions.

TABLE 5**Characteristics of Catheter Tip Sites in the Extravasation Group (n = 26)**

		Positive	%	False Negative	%
Course of the vein	Straight	2	9.1	1	25.0
	Confluence	11	50.0	2	50.0
	Branch	6	27.3	1	25.0
	Confluence and branch	3	13.6	0	0.0
	Others	0	0.0	0	0.0
	Unknown	0	0.0	0	0.0
Bony prominence	Prominence	2	9.1	1	25.0
	Nonprominence	20	90.9	3	75.0

The present findings demonstrate that thermography can be used to diagnose extravasation of antineoplastic agents more accurately than conventional macroscopic assessment. The use of thermography allows detection of extravasations that previously were overlooked, thus helping maintain and improve the quality of life of cancer patients undergoing chemotherapy. The clinical application of thermography for early detection of extravasation would decrease the incidence of ulceration, nerve damage, and other cases of severe skin damage resulting from extravasation of antineoplastic agents.

The method of handling thermography is straightforward. The time taken for each image is less than 10 seconds. For these reasons, the assessment or diagnosis of extravasation using thermography can be used as part of the infusion procedure in chemotherapy.

The hospital in which this study was conducted could be described as a typical outpatient chemotherapy center in Japan. As a designated regional cancer center, the hospital provides standardized therapy based on treatment guidelines. The results of this study could therefore be extrapolated to a common outpatient chemotherapy setting in Japan.

This study had 2 key limitations. The first was the lack of a “gold standard” for diagnosing extravasation. The study did not involve direct assessment of extravasation using ultrasonography or other modalities. Because methods for assessing extravasation are currently lacking, this study used observation during administration and subsequent cutaneous symptoms as secondary end points. Thus, the nonextravasation group may have included patients who experienced extravasation, but displayed no subsequent cutaneous symptoms. The second limitation of the study was the inadequate consideration of the limits of extravasation diagnosis because of the small number of false-negative results. Therefore, a larger study population is needed in future research.

CONCLUSION

This study evaluated the predictive validity of thermography for identifying extravasation during antineoplastic infusion therapy. Temperature decrease per centimeter from margin to center of low-temperature regions is usable as a determination index.

A low-temperature region with a gradual decline in temperature from the infusion site margin was seen in the extravasation group. The AUC for detecting extravasation using this decrease in temperature at the margin of the

low-temperature region as an indicator was 0.94. The optimal cutoff for the decrease in temperature to predict extravasation was considered to be $< 0.7^{\circ}\text{C}/\text{cm}$, offering 84.6% sensitivity, 94.8% specificity, and positive and negative predictive values of 64.7% and 98.2%, respectively. The study findings demonstrate that thermography can be used for more accurate diagnosis of extravasation of antineoplastic agents compared with conventional macroscopic assessment.

Cases in which thermography was incapable of diagnosing extravasation were characterized by a combination of vein bifurcation and confluence, and the location of the vein over a bony prominence.

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