

LABELING

Onco-LIFE™ Labeling Summary

Onco-LIFE Endoscopic Light Source and Video Camera Components

Device Components		Specifications
Light Source (Model OLLS)	Lamp type	150 W super-high-pressure mercury arc lamp
	Dimensions	430 mm x 300 mm x 135 mm
Camera (Model OLCA)	Dimensions	95 mm x 65 mm x 65 mm
	Weight	300 g
Camera Controller (Model OLCC)	Dimensions	430 mm x 300 mm x 135 mm
	Weight	5.5 kg
Required Accessory	Color Reference Standard	

Device Description

Onco-LIFE consists of an endoscopic light source and video camera for use with conventional endoscopes. Onco-LIFE operates in two imaging modes: conventional white light imaging mode (also referred to as color imaging mode) and fluorescence imaging mode. In the white light mode, Onco-LIFE functions in the same way as currently marketed conventional endoscopic light sources and cameras.

In the fluorescence mode, Onco-LIFE functions in a similar manner to the Xillix LIFE-Lung™ Fluorescence Endoscopy System (PMA P950042) and images native tissue fluorescence to aid in the identification of potentially precancerous and cancerous tissue. Blue light is used to illuminate the tissue and excite fluorophors naturally present in the tissue. A real-time video image of the fluorescing tissue is acquired and displayed on the video monitor. Areas suspicious for disease are displayed in red in the video image.

Indications for Use

This device is indicated for use with fluorescence imaging during bronchoscopy as an adjunct to white light imaging, to detect and localize tissue suspicious for moderate or severe dysplasia, carcinoma *in situ*, or invasive cancer in patients with suspected or previously treated lung cancer.

Contraindications for Use

Onco-LIFE should not be used with patients who are contraindicated for bronchoscopic examination. Contraindications typically include uncontrolled hypertension, unstable angina and/or known uncontrollable bleeding disorders.

For fluorescence examination, additional contraindications may include recent use of photosensitizing drugs, chemopreventative drugs, systemic cytotoxic chemotherapy agents and/or ionizing radiation treatment.

Safety Warnings when Using Onco-LIFE

- Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
- Onco-LIFE is only to be used by licensed endoscopists with appropriate training and skill in flexible fiberoptic endoscopy and who have been trained in the use of Onco-LIFE. The physician should use his/her judgment and experience in interpreting the fluorescence images.
- Physicians with red/green color blindness may be unable to fully utilize fluorescence imaging, to distinguish subtle color differences associated with abnormal bronchial tissue.
- Safety and effectiveness of Onco-LIFE has not been evaluated in pregnant women or pediatric application.
- The physician should perform a complete white light bronchoscopy, then repeat the examination using fluorescence. Because blood may mask the autofluorescence image, the physician should perform the biopsy procedure, moving from distal to proximal, only after completing both examinations.
- Onco-LIFE is intended to aid physicians in identifying and localizing abnormal bronchial tissue for biopsy. Biopsies may be retrieved in either white light or fluorescence modes. All final diagnoses are determined by histological review.
- Onco-LIFE may display fluorescence images that could be incorrectly interpreted by the physician. Images that appear bronchoscopically positive may be caused by inflammation, scope or suction trauma, scar tissue, the presence of photosensitizing agents or chemopreventive agents. Images that appear bronchoscopically negative may not always accurately indicate the absence of abnormal tissues, i.e., not all abnormal bronchial tissue will be detected.
- The presence of acute pulmonary infection, including bronchitis and pneumonia, may increase the risks associated with bronchoscopy and the risk of obtaining false positive readings from this examination.

Additional warnings and precautions for use of Onco-LIFE are listed under “General Warnings” in the Instructions for Use & Operator’s Manual.

Summary of Clinical Study OL-L01

Onco-LIFE provides both a conventional white light (WL) imaging mode and a fluorescence (FL) imaging mode in a single endoscopic imaging device. The Onco-LIFE pivotal study OL-L01 was designed to evaluate the safety and effectiveness of the device. Physicians used fluorescence as an adjunct to white light imaging and conducted the study using white light examination followed by fluorescence examination.

A total of 204 patients (137 male, 66 female, N=203 plus 1 patient who withdrew consent) were enrolled in the study at seven participating clinical centers. All 204 enrolled patients were considered evaluable for safety. No adverse events (AEs) attributable to Onco-LIFE or unanticipated adverse device events (UADEs) were observed during this clinical study.

Of the 204 enrolled patients 34 were excluded from the efficacy analyses, (due to training cases, incomplete data, etc.) resulting in 170 evaluable patients. In the Onco-LIFE study 68% of the patients evaluated were male (32% female), the mean age was 61.7 years (range 45 – 75 years), 99%

were current or former smokers. These patient demographics are consistent with the patient population at risk for lung cancer. The 170 patients included in the efficacy analyses had a total of 864 biopsies, of which 776 biopsies (90%) were considered evaluable and 88 biopsies were excluded. The per-lesion and per-patient sensitivity and false positive rate (1 – specificity) analyses are described below. Although sensitivity and 1 – specificity were overestimated (intrinsically their denominators are undercounted), for each quantity the relative estimate (the ratio of WL + FL to WL alone) is an unbiased estimate of the true ratio.

- Per-lesion relative sensitivity analysis
 - Including invasive cancer WL sensitivity is 0.47 and WL+FL sensitivity is 0.71. The relative sensitivity is 1.50, indicating that the addition of an Onco-LIFE FL examination to WL bronchoscopy resulted in a 50% increase in detection of positive lesions including invasive cancer. The 95% 1-sided confidence limit is 1.29. This exceeds the requirement for clinical significance (1.15) as set by the protocol. Thus the combination of WL+FL shows both statistically and clinically increased sensitivity over WL alone.
 - Excluding invasive cancer WL sensitivity is 0.10 and WL+FL sensitivity is 0.44. The relative sensitivity is 4.25, indicating that the addition of an Onco-LIFE FL examination to WL bronchoscopy resulted in a 325% increase in the detection of moderate/severe dysplasia or *CIS* lesions. The 95% 1-sided confidence limit is 2.22. This exceeds the requirement for clinical significance (1.15) as set by the protocol. Thus the combination of WL+FL shows both statistically and clinically increased sensitivity over WL alone.
- Per-patient relative sensitivity
 - Including invasive cancer WL sensitivity is 0.56 and WL+FL sensitivity is 0.74. The relative sensitivity is 1.33, indicating that the addition of an Onco-LIFE FL examination to WL bronchoscopy resulted in a 33% increase in the detection of patients with precancerous and cancerous lesions. The 95% 1-sided confidence limit is 1.15. This meets the requirement for clinical significance (1.15) as set by the protocol. Thus the combination of WL+FL shows both statistically and clinically increased sensitivity over WL alone.
 - Excluding invasive cancer WL sensitivity is 0.16 and WL+FL sensitivity is 0.56. The relative sensitivity is 3.50, indicating that the addition of an Onco-LIFE FL examination to WL bronchoscopy resulted in a 250% increase in the detection of patients with moderate/severe dysplasia or *CIS*. The 95% 1-sided confidence limit is 1.86. This exceeds the requirement for clinical significance (1.15) as set by the protocol. Thus the combination of WL+FL shows both statistically and clinically increased sensitivity over WL alone.
- Per-lesion relative False Positive Rate (1 – Specificity)
 - Including invasive cancer WL 1-Specificity is 0.07 and WL+FL 1-Specificity is 0.26. The ratio of 1-Specificity was 3.56 (95% CI 2.7, 4.9), indicating an increase in the false positive rate found with WL+FL compared to WL alone. These additional positive lesions were associated with an increase in the number of false positive biopsies. This increase in the false-positive rate is consistent with increased false-positive rates in other studies, for example the Xillix LIFE-Lung study reported a 1-Specificity of 3.40.

Summary of Onco-LIFE Study OL-LO1 Clinical Results

Per Protocol

(N=170 patients, final pathology)

Per-Lesion Sensitivity	WL	WL+ FL	Relative Sensitivity	95% 1-sided Confidence Lower Limit
Includes Invasive Cancer	0.47	0.71	1.50 (50% improvement)	1.29
Excludes Invasive Cancer	0.10	0.44	4.25 (325% improvement)	2.22
Per-Patient Sensitivity	WL	WL+ FL	Relative Sensitivity	95% 1-sided Confidence Lower Limit
Includes Invasive Cancer	0.56	0.74	1.33 (33% improvement)	1.15
Excludes Invasive Cancer	0.16	0.56	3.50 (250% improvement)	1.86
Per-Lesion 1-Specificity	WL	WL+ FL	Ratio of 1-Specificity	95% 1-sided Confidence Upper Limit
Includes Invasive Cancer	0.07	0.26	3.56	4.41

Gender-Based Analysis

In the Onco-LIFE study 68% of the patients evaluated were male (32% female), the mean age was 61.7 years (range 45 – 75 years), 99% were current or former smokers. These patient demographics are consistent with the patient population at risk for lung cancer.

Relative sensitivity of Onco-LIFE was 1.62 in males and 1.33 in females. While the relative sensitivity was higher in males, there was no statistically significant difference ($p = 0.38$) between the gender-based cohorts, indicating that Onco-LIFE was equally effective for both gender groups. Ratio of 1-specificity was similar in both gender groups (3.25 in males, 3.61 in females, $p = 0.81$).

Age-Based Analysis

Median age in the study population was 62 years. Patients were stratified for analysis by less than or equal to 62 years of age and greater than age 62. Relative sensitivity of Onco-LIFE was 1.63 in patients 62 years or younger and 1.40 in patients older than 62 years of age. While the relative sensitivity was higher in the 62 years and younger patient subgroup, there was no statistically significant difference ($p = 0.57$) between the age groups, indicating that Onco-LIFE was equally effective for both age groups. Ratio of 1-specificity was better in the greater than 62 patient population (2.74 as compared to 5.24 in the 62 years and younger age group). The difference is statistically significant ($p = 0.009$), indicating that fewer false positive biopsies were obtained from patients greater than 62 years of age.

Safety Warnings and Precautions at the Site of Installation

- Do not use or store liquids around the Onco-LIFE light source or camera controller. If liquid enters the Onco-LIFE light source or camera controller, immediately switch off all Onco-LIFE components and unplug them from power outlets.
- Do not insert objects into the ventilation holes of the light source or camera controller enclosures.
- Do not attempt to remove the covers from the Onco-LIFE light source and camera controller. Refer all servicing to a recognized Xillix service representative.
- Connect Onco-LIFE to “Hospital Only” or “Hospital Grade” power outlets.
- Connect Onco-LIFE only to approved medical devices or to devices that are powered from approved isolation transformers.
- The patient leakage currents from multiple, simultaneously used, energized endoscopic accessories may be additive. Use Onco-LIFE with energized endoscopic accessories that minimize the leakage current to the patient.
- Do not use Onco-LIFE if the power cords or plugs are damaged or modified in any way. Unplug power cords by grasping the plug. Do not unplug power cords by pulling on the cable. Unplug the power cords from the power outlet if Onco-LIFE is not to be used for an extended period. Do not remove or override the ground connection on the power cords.
- Possible explosion hazard. Do not use Onco-LIFE in the presence of
 - High oxygen concentrations (O₂).
 - Oxidizing agents such as nitrous oxide (N₂O).
 - Flammable anesthetics.
- Do not use Onco-LIFE if any part of the device is damaged or does not function properly. Failure to follow this warning may lead to injury. Do not attempt to remove the covers from the Onco-LIFE light source and camera controller. Refer all servicing to service personnel recognized by Xillix Technologies Corp.
- Follow the procedures described in Chapter 5 of the Instructions for Use & Operator’s Manual to clean and disinfect Onco-LIFE and accessories.
- Avoid looking at light emitted directly from the endoscope. Protect the patient’s eyes from accidental light exposure when inserting and removing the endoscope during endoscopy.

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